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BRITISH MEDICAL JOURNAL

LONDON SATURDAY MAY 29 1954

A COMPARISON OF CORTISONE AND ASPIRIN IN THE TREATMENT OF EARLY CASES OF RHEUMATOID ARTHRITIS

A REPORT BY THE JOINT COMMITTEE OF THE MEDICAL RESEARCH COUNCIL AND NUFFIELD FOUNDATION ON CLINICAL TRIALS OF CORTISONE, A.C.T.H., AND OTHER THERAPEUTIC MEASURES IN CHRONIC RHEUMATIC DISEASES

In 1951 the Medical Research Council and Nuffield Foundation Joint Committee on Clinical Trials of Cortisone, A.C.T.H., and Other Therapeutic Measures in Chronic Rheumatic Diseases decided that, for an effective assessment of the value of cortisone within its field of study, it was essential to carry out relatively small-scale but carefully controlled clinical trials. One of these trials, it was agreed, should deal with the important problem of the treatment of patients in the early stages of rheumatoid arthritis. The aim would be to measure the therapeutic effects of cortisone treatment upon the rheumatoid process while that process is still uncomplicated, either by severe anatomical changes in the joints or by metabolic or endocrine disturbances resulting from a prolonged and debilitating disease. In short, such a trial would have two objects: first, to compare the relative efficacy of cortisone and another drug usually regarded as efficacious in relieving symptoms and in improving the patient's functional capacity; and, secondly, to study the evolution of the rheumatoid process during prolonged therapy with these different agents. A scheme for this trial was drawn up by a subcommittee of the Joint Committee, and six centres in England and Scotland agreed to take part.*

Type of Patient

It was agreed that the patients to be included in the trial must (*a*) be within the ages of 2 to 59 years inclusive; (*b*) have a polyarthritis of rheumatoid type affecting at least four joints and bilateral involvement of either hands or feet, ankles, or wrists; and (*c*) have had the disease at their time of entry to the trial for not less than three months and not more than nine months. In deciding upon this duration it was required that the initial symptoms of the present illness, which had brought the patient to the centre, should be the first evidence of any rheumatoid disease in the patient—except that a previous episode of polyarthritis suggestive of rheumatoid disease would not exclude the patient from the trial provided that this episode had been of less than 12 months' duration, had left no residual signs, and had resolved completely at least one year before the onset of the present illness. A previous history of a painful incident of up to three weeks' duration would not be considered evidence of previous rheumatoid disease.

No other diagnostic criteria were considered necessary, but centres were asked to make every effort to exclude other diseases such as rheumatic fever, Reiter's disease, and neisserian infection. In addition the sheep-cell agglutination test first described by Rose *et al.* (1948) was performed in most of the patients, and usually on several occasions.

Allocation to Treatment

In a long-term trial of this nature it was obviously out of the question, on ethical grounds, to set up a control group on a dummy treatment. The contrast must lie between treatment by cortisone and another drug usually regarded as efficacious in the treatment of rheumatoid arthritis. The two modes of treatment adopted, and allocated at random, were therefore (1) cortisone and (2) aspirin, with both groups receiving the same basic regime of splints, physiotherapy, etc. No patient would, of course, be brought into the trial unless he or she could be regarded as a suitable case for treatment by *either* of these agents.

Because clinicians at the participating centres would have to select patients for admission to the trial it was necessary to ensure that they would not know whether each patient, in the event of being brought in, would be on cortisone or on aspirin. The procedure adopted was as follows. The clinician at the centre accepted a patient as suitable on the basis of the criteria laid down. Having done so he applied to a central office to know whether the treatment of that patient should be with cortisone or aspirin. At the central office a register had been constructed showing the order in which the

*The members of the Joint Committee are: Sir Henry Cohen (chairman), Dr. E. G. L. Bywaters, Dr. W. S. C. Copeman, Sir Charles Dodds, Dr. J. J. R. Duthie, Professor A. Bradford Hill, Mr. H. Osmond-Clarke, Dr. F. T. G. Prunty, Dr. J. Reid, Dr. H. F. West, Professor J. H. Kellgren and Mr. W. A. Sanderson (joint secretaries).

The Subcommittee and participating centres were: Professor J. H. Kellgren (chairman), Rheumatism Research Centre, Manchester; Dr. E. G. L. Bywaters, Postgraduate Medical School of London and Canadian Red Cross Memorial Hospital, Taplow; Dr. W. S. C. Copeman, West London Hospital; Dr. J. J. R. Duthie, Northern General Hospital, Edinburgh; Dr. H. F. West, Sheffield Centre for the Investigation and Treatment of Rheumatic Diseases; Professor A. Bradford Hill; and Dr. F. T. G. Prunty.

The Subcommittee was assisted at these centres by the following workers, to whom it expresses its thanks: Dr. B. Ansell, Dr. C. K. Crawford, Dr. G. Fearnley, Dr H. Lackner, Dr. I. Meanock, Dr. J. Redmill, Dr. O. A. Savage, Dr. J. Sharp, and Dr. M. Thompson.

The results of the trial were analysed by Dr. J. T. Boyd, of the Statistical Research Unit of the Medical Research Council, London School of Hygiene and Tropical Medicine, and the Subcommittee is greatly indebted to him for his work.

treatments were to be applied. It was held by one person. Such a random order of treatments was constructed separately for each of 48 small subgroups of patients—namely, according to whether they were (*a*) male or female, (*b*) aged 2–16 or 17–59 years, (*c*) had a duration of symptoms of three to five months or seven to nine months, and (*d*) were treated at one or other of the six centres. Within each of these small subgroups random sampling numbers were used to give approximately equal numbers of patients on cortisone and aspirin. In summation, therefore, the cortisone and aspirin groups would be very similar in these four characteristics—sex, age, duration of illness, and treatment centre.

In detail, the technique was that on admitting a patient a treatment centre would send particulars of the sex, age, and duration of illness to the holder of the register. The prepared list for a person of that sex, age, and duration would be consulted, the patient's name entered on the next available line, and the nature of the treatment already inscribed on that line would, with supplies of hormone or aspirin, be sent to the treatment centre.

Treatment

Each patient was admitted to hospital for a minimum period of four weeks, but subsequently could be treated and observed as an out-patient. It proved impossible to make up cortisone and aspirin suspensions to look alike. The aspirin was therefore given in brown tablets with a bitter flavour so that they would be unrecognizable by the patient as "merely aspirin." They were labelled "Tabs. Rheumatic C."* Cortisone acetate was given orally either in tablet form or as a suspension made up in syrup. It was labelled "Tabs. (or Mist.) Rheumatic A." Patients were asked not to take additional drugs or tablets. For the first year of treatment it was laid down that therapy would be given in twelve-weeks courses separated by one week off treatment. Each course would start with a standard dosage, after which the physician was free to adjust the dose to suit the requirements of individual patients. The specified courses for adult patients, given in divided doses not fewer than three times a day, were as follows :

		Cortisone	*Aspirin*
First week:	Day 1	300 mg. ..	6 g.
" "	" 2	200 " ..	6 "
" "	" 3 to day 7 ..	100 " daily	6 " daily
Second week:	" 8 " " 14 ..	50 " "	2 " "
Third to twelfth week:	" 15 " " 84 ..	Individualized at 25 to 200 mg. daily with graded withdrawal in week 12	Individualized at 1 to 8 g. daily with graded withdrawal in week 12

In the "free" period—that is, the third to twelfth week—the physician was asked to employ the minimum dosage that would restore maximal functional efficiency without producing serious side-effects. In the thirteenth week no treatment by cortisone or aspirin was given, observations and measurements being made (in this week analgesics other than aspirin could, if necessary, be given). If symptoms recurred the twelve-weeks course was repeated, except that the selected dose for the individual patient replaced the standard dose of the second week.

Assessment of Patient

Clinical assessment of each patient (including measurement of the haemoglobin level and blood sedimentation rate) was required one week before and also immediately before the start of treatment. After therapy had begun, an assessment of some or all characteristics was called for at the end of the first, second, fourth, eighth, twelfth, and thirteenth weeks of the first course, and at the end of the first, eighth, and thirteenth weeks of the second and subsequent courses.

The clinical assessment included (*a*) a defined judgment of the patient's general functional capacity (for the five grades laid down, see Table VII); (*b*) a judgment of the activity of the disease as inactive, slightly active, or very active; and (*c*) a statement whether the patient appeared to be in remission. In addition to these subjective assessments the clinician was required to measure the strength of grip for each hand. (The patient had to squeeze an oblong rubber bag 5 by 3 in. (12.5 by 7.5 cm.) inflated at a pressure of 10 mm. Hg, and the figure recorded was the average of three grips.) Two tests of dexterity were applied—namely, in patients with affected hands the time taken to tie six double knots with 12-in. (30-cm.) pieces of household string, and in patients with affected legs the time taken to go up and down ten steps. Estimates were also made of joint tenderness and of range of movement, and the number and site of any new joints involved were recorded as well as of previously affected joints which had recovered. Complications and side-effects were noted. The only obligatory laboratory tests were the blood sedimentation rate and the haemoglobin level.

The Analysis of the Data

In total, 62 adult patients (aged 17 to 59) and 14 children were admitted to the trial. The latter are too few to be informative, and the present report is confined to the adult group. One of these patients, allotted to the aspirin group, refused to co-operate, so that the numbers available are 30 on cortisone and 31 on aspirin. In 53 cases the results of a sheep-cell agglutination test are available. They are lacking for three patients on aspirin who were lost to the trial at an early stage (see below) and for five other patients who were followed up for the first year but never tested (three on aspirin and two on cortisone). The cases admitted at Edinburgh, Sheffield, and Manchester were tested by the method of Ball (1950), the test being regarded as positive if agglutination occurred in a titre of 1:4 or higher when read at one hour, or 1:32 or higher when read at 18 hours : a positive result was obtained on at least one occasion in 29 out of 40 patients (73%). The cases admitted at Hammersmith and West London were tested by the original method of Rose, in which the test is considered positive if the two titres recorded show a ratio of 1:16 or higher : in 9 out of 13 cases a positive result was obtained on at least one occasion (69%). In view of the close similarity of the results given by the two methods the data from the different centres may be added in comparing the two treatment groups. It is then found that 18 of the 28 patients on cortisone who were tested were positive at one time or another (64%), and 20 of the 25 patients on aspirin who were tested (80%). In other words, each treatment group had a high proportion of positive tests and there is no statistically significant difference between them.

Ball, whose method was principally used in this trial, has reported 50% of positive results in a large unselected series of out-patients diagnosed as suffering from rheumatoid arthritis; and in a carefully selected series of typical cases of varying duration admitted to the Manchester Royal Infirmary for special study 41 out of 61 (67%) gave a positive test (Ball, 1952). Scott (1952), using the Rose method, has reported positive results (a ratio of 1:16 or more) in 60% of an unselected series of 124 confirmed rheumatoid arthritis patients. The 38 positive results in 53 patients in the present trial (72%) compare very favourably with these various figures. They are good evidence of the accuracy of the diagnosis of rheumatoid arthritis in the patients admitted to the trial.

Details of the patients by centre, sex, age, and duration of symptoms are given in Table I. The data show how effective the method of allocation has been in equalizing the two treatment groups in these respects. Their initial equalities or inequalities in other characteristics will be seen

*The Committee is indebted to Mr. J. B. Lloyd, chief pharmacist at the Manchester Royal Infirmary, for the preparation of the tablets.

TABLE I.—*Comparison of the Patients on Cortisone and Aspirin at Start of Treatment*

Treatment Centre	No. of Patients on			Male		Female	
				No. of Patients on		No. of Patients on	
	Cortisone	Aspirin		Cortisone	Aspirin	Cortisone	Aspirin
1	2	5	Age: 17–39 years	5	5	4	6
2	5	4	40–59 „	8	6	13	14
3	1	—	Total	13	11	17	20
4	8	8					
5	6	6	Duration of symptoms: 3–5 months	5	4	6	8
6	8	8	7–9 „	8	7	11	12
Total	30	31	Total	13	11	17	20

in each of the tables that follow, where these initial assessments are set alongside the subsequent observations.

It must be noted that during the first year of treatment and observation three patients, all on aspirin, were lost to sight. The reasons were as follows :

(1) Male aged 48, West London Centre. After some preliminary improvement his condition deteriorated and he did not, after six months, feel that he was gaining any benefit from the tablets.

(2) Female aged 53, Sheffield Centre. Relapsed on leaving hospital, had a psychological breakdown and declined to return (at week 12).

(3) Female aged 60, Edinburgh Centre. Left the country for New Zealand (at week 30).

The first two must clearly be counted as failures of treatment and must be remembered in considering the results. The third patient was responding satisfactorily up to week 30, and subsequent information has confirmed that she continues to do well on aspirin. For the remaining 58 patients assessments were available towards the end of the first year. The centres, however, were not able invariably to fulfil the agreed schedule, and it was found that the number of patients off treatment in week 52, as required by it, was not sufficient to allow an effective analysis at that point (only about half had the off-treatment week at the end of the year). On the other hand, assessments were available for all 58 patients at some point close to the end of the year while they were still on their personal dosage. The week chosen for analysis, therefore, was, for each patient, that week of personal dosage which provided assessments and was nearest to week 52—with the proviso that it must lie at least four weeks before an off-treatment week—that is, before any "tapering off" of dosage would have begun. There were six patients (four on cortisone and two on aspirin) who at the end of the year had been off treatment for periods varying from 9 to 26 weeks. In these cases the personal dosage was taken to be nil and the week nearest to the end of the year was chosen for inclusion. The actual points taken lay between the 46th and 54th week in all but three cases (which were at the 42nd, 44th, and 45th week).

Results

(a) Joint Tenderness

The changes in joint tenderness are shown in Table II. In reaching the figures there set out an overall "tenderness" index was first computed separately for each patient by taking the average of his recorded joints. The mean of these averages gave, at each point of time, an index for the treatment group as a whole. It will be seen that the average position at the start of treatment is almost identical in the two groups—1.91 cortisone and 1.89 aspirin. In both there is a significant and considerable reduction in pain in the first week of treatment, when the averages fall by 0.80 and 0.72 respectively. This fall continues, though more slowly, up to week 8, and very slightly thereafter, between week 8 and the end of the year. As a result the final averages are still almost identical, though at a much lower level (0.74 cortisone and 0.76 aspirin); the percentage reduction over the year has been some 60% in each group.

TABLE II.—*The Average Changes Observed in the Joint Tenderness Index**

Joints Measured	Treatment Group	Average Joint Tenderness in Week 0	Average Changes in Joint Tenderness			Joint Tenderness at 1 Year	
			Week 0 to Week 1	Week 1 to Week 8	Week 8 to 1 Year	Average	As % of Average at Week 0
All relevant joints (including wrist and hand, given below)	Cortisone	1·91	*−0·80*†	*−0·29*	−0·09	*0·74*	39
	Aspirin	1·89	*−0·72*	−0·21	−0·15	*0·76*	40
Wrist-joints	Cortisone	1·80	*−0·83*	−0·10	+0·13	*1·00*	56
	Aspirin	1·93	*−0·79*	−0·21	+0·08	*0·96*	50
Small joints of hand	Cortisone	2·25	*−0·93*	*−0·50*	−0·25	*0·58*	26
	Aspirin	2·05	*−0·82*	−0·24	−0·34	*0·53*	26

* Tenderness was graded on the scale 0 for no pain, 1 for slight pain, 2 for wincing, and 3 for wincing and withdrawal. The records have been used as an ordinary numerical scale.

† In this and subsequent tables, values in italics are statistically significant changes between specified times, and in the penultimate column between the beginning and end of the year ($P<0.05$).

In the second and third rows of Table II similar figures are given separately for the wrist-joints and the small joints of the hand. Though the changes are not statistically significant, it appears that with each of the treatments the average levels of pain tended to continue to decrease up to the end of the year in respect of the small joints of the hand, but to show some increases after week 8 in the wrist-joints. In both instances, however, the initial and final averages are closely similar for the cortisone- and aspirin-treated groups.

(b) Range of Movement and Strength of Grip

Table III gives the figures for range of movement in the wrists and strength of grip. In these respects the cortisone group reveals, by chance, some advantage before treatment was started—the average range of movement and average strength of grip were greater. (The difference in the average range of movement is statistically significant.) It is not possible, however, to detect any material difference between the two groups in their responses to treatment. There is, in each characteristic, a substantial improvement in the first week of treatment; week 1 to week 8 and

TABLE III.—*The Average Changes in (a) Range of Wrist Movement and (b) Strength of Grip*

Characteristic Measured	Treatment Group	Average Measurement in Week 0	Average Changes in Measurement			Measurement at 1 Year	
			Week 0 to Week 1	Week 1 to Week 8	Week 8 to 1 Year	Average	As % of Average at Week 0
Range of wrist movement (in degrees)	Cortisone	99*	*+13·9*	+4·6	+1·1	*120**	121
	Aspirin	78	*+23·2*	−1·8	+2·3	*103*	132
Strength of grip (in mm. Hg) left hand	Cortisone	138	*+33·3*	+17·8	+12·2	*202**	146
	Aspirin	111	*+35·3*	+8·5	+0·4	*164*	148
Strength of grip (in mm. Hg) right hand	Cortisone	134	*+46·7*	+2·5	+3·7	*187*	140
	Aspirin	116	*+34·5*	+15·1	−7·1	*166*	143

* The mean of the cortisone group was significantly greater than the mean of the aspirin group.

week 8 to 1 year reveal, on the whole, some further increases, but the changes are much smaller and very variable At the end of the year the average for the cortisone group, compared with the aspirin group, is significantly greater for the range of movement in the wrists but by no more than it was initially. In respect of strength of grip the averages for the cortisone group at the end of the year are also above those for the aspirin group, but once again by no more than they were initially. In other words, the mean percentage changes have been remarkably similar—an increase of 20–30% in range of wrist movement and of 40–50% in strength of grip.

(c) Tests of Dexterity

Table IV gives the results of the timing tests. The average starting-points of the two groups are reasonably alike, and the progression under treatment and the end-results are again very similar. Each treatment group shows an average improvement of some 20–25%.

TABLE IV.—*The Average Changes in Time Taken to (a) Tie Six Knots and (b) Go Up and Down Ten Steps, by Patients With Affected Hands and Legs Respectively*

Characteristic Measured	Treatment Group	Average Measurement in Week 0	Average Changes in Measurement			Measurement at 1 Year	
			Week 0 to Week 1	Week 1 to Week 8	Week 8 to 1 Year	Average	As % of Average at Week 0
Time (in seconds) to tie 6 knots	Cortisone	38	*−4·2*	−0·2	*−4·2*	29	76
	Aspirin	41	*−3·0*	−3·9	−0·8	34	83
Time (in seconds) to go up and down 10 steps	Cortisone	14	−1·3	−2·6	+0·6	11	79
	Aspirin	18	−4·5	+0·8	−0·2	13	72

(d) Haemoglobin Level and Blood Sedimentation Rate

The changes in the level of haemoglobin and in the blood sedimentation rate are shown in Table V. In both these respects there is apparent some difference between the cortisone- and aspirin-treated groups. In haemoglobin level they start alike with mean values of 12.2 and 12.1 g.%. Under treatment the patients on cortisone show, on the average, an improvement, and at the end of the year the mean has reached 13.1 g.%. The corresponding changes under aspirin are erratic and statistically insignificant, with the final average of 11.3 g.%, rather below the initial level and significantly below the average for the cortisone group.

TABLE V.—*The Average Changes in (a) Haemoglobin and (b) Blood Sedimentation Rate*

Characteristic Measured	Treatment Group	Average Measurement in Week 0	Average Changes in Measurement			Measurement at 1 Year	
			Week 0 to Week 1	Week 1 to Week 8	Week 8 to 1 Year	Average	As % of Average at Week 0
Haemoglobin (in g.%)	Cortisone	12·2	+0·2*	*+0·6*	+0·1*	*13·1**	107
	Aspirin	12·1	−0·4	+0·4	+0·8	11·3	93
E.S.R. (mm./hr.)	Cortisone	42	−18·1*	−4·4	+5·5	27	64
	Aspirin	42	−1·4	+0·4	−6·1	35	83

* The averages shown by the cortisone and aspirin groups differ significantly.

The mean blood sedimentation rate at the start of treatment was identical—42 mm./hour in each group. In the first week of treatment there was a pronounced fall in the cortisone group and an insignificant fall in the aspirin group. Subsequent mean changes were slight, and at the end of the year of observation the final averages of 27 mm./hour for patients on cortisone and 35 mm./hour for patients on aspirin do not differ appreciably, though still slightly favouring the former group. On the other hand, in each treatment group five patients had a value of 10 mm./hour or below at the end of the year.

(e) Clinical Assessments

At the end of the year two patients on cortisone and three on aspirin were reported to be in remission (though two of those on aspirin were still on maintenance doses of 4 g. and 1.7 g. respectively). There were a further two patients on cortisone and a further one on aspirin who had not been on treatment for 10, 40, and 20 weeks respectively. Thus four patients in each group were regarded as either in remission or as not requiring treatment at that time. The overall assessments of condition and progress at the end of the first year are shown in Table VI, and reveal little difference between the two groups. If the two aspirin patients who progressed unfavourably and were lost to view are included as "very active" the picture would not be materially altered.

TABLE VI.—*Clinical Assessments of Activity at One Year*

Grade	Cortisone No.	Aspirin No.
Inactive	2	2
Slightly active	21	19
Very „	7	7
Total	30	28

The assessments of functional capacity are given in Table VII, and once again the two treatment groups are more remarkable for their similarity than for their dissimilarity. At the start of treatment the majority of patients were placed in grade 3—not employed and unemployable, no physical recreations. By the eighth week many had been moved to the higher grades—full or light work, etc. In the week off treatment, the thirteenth, a number returned to the lower grades, but by the close of the year about four-fifths of the patients were capable of either full (grade 1) or light work (grade 2). Division of these patients into grades 1 and 2 separately gives 13 and 10 patients on cortisone and 11 and 10 on aspirin, or approximately 40%, with full functional capacity in each treatment group. Only two patients, both on cortisone, were bedridden at the end of the year. The two missing aspirin cases may be set against these—that is, putting the most unfavourable complexion upon them.

TABLE VII.—*Number of Patients with Given Functional Capacity at Different Points of Treatment**

Treatment Group	Time of Assessment	Functional Capacity			Total
		1 or 2	3	4 or 5	
Cortisone ..	Week 0	4	18	8	30
Aspirin ..		5	18	6	29†
Cortisone ..	„ 8	18	11	1	30
Aspirin ..		15	11	3	29
Cortisone ..	„ 13	10	16	4	30
Aspirin ..		10	13	5	28
Cortisone ..	1 year	23	5	2	30
Aspirin ..		21	5	0	26

* Functional capacity grades were:
Grade 1: Fully employed or employable in usual work and able to undertake normal physical recreation.
„ 2: Doing light or part-time work and only limited physical recreation. For housewives, all except the heaviest housework.
„ 3: Not employed and unemployable. No physical recreations. Housewives, only light housework and limited shopping.
„ 4: Confined to house or wheel-chair, but able to look after themselves in essentials of life. Hospital patients confined to bed.
„ 5: Completely bedridden.

† No record was made in this respect for two patients, and, as stated previously, three were subsequently lost to view.

(f) Side-effects

Side-effects were recorded for 19 patients in the cortisone group and 21 patients in the aspirin group. Most of these patients had more than one complication, the most frequent in the cortisone group being moon-face or rubicundity (11 patients), depression (5 patients), and euphoria (4 patients), and in the aspirin group tinnitus (11 patients), deafness (10 patients), nausea, dyspepsia, or anorexia (13 patients). There were no severe complications in the cortisone group necessitating discontinuance of treatment despite a final personal dosage at the end of the year of between 100 and 125 mg. a day in 11 of the 26 patients.

The numbers of patients showing side-effects in each consecutive three months of this first year's treatment were 14, 15, 11, and 12 in patients on cortisone, and 16, 10, 6, and 6 in patients on aspirin. In other words, the numbers with these minor complications were equal in the early months of treatment, but became less in the aspirin group as time passed.

Discussion

This trial, as emphasized in the early paragraphs of the report, was designed to answer a specific but very important question—namely, in early and uncomplicated cases of rheumatoid arthritis is it possible to maintain the patient's well-being more efficiently by treatment with cortisone than by treatment with aspirin? Simultaneously, if the trial can be continued into a second or third year, as is envisaged, light may be thrown upon the evolution of the rheumatoid process during prolonged therapy with these different agents. While scientifically it would obviously be of much value to be able to compare the changes in both these treated groups with those taking place in a group receiving neither cortisone nor aspirin, ethically such a course is impossible. One or other agent, it was held, must be administered—together with any other basic treatment that might be required (splints, physiotherapy, etc.).

It was, however, decided that treatment should be tapered off at the end of each three-months period and then withheld for one week to allow of assessment of the patient's condition. Analysis of the data thus provided at the end of the first course—that is, at the thirteenth week—revealed a distinct "relapse" in some of the patients, though an equal degree of "relapse" occurred on the two forms of treatment. For example, the average joint tenderness at the start of treatment was 1.91 in the cortisone group and 1.89 in the aspirin group (see Table II). By week 8 the average had declined by 1.09 in the cortisone group and by 0.93 in the aspirin group. In the week off treatment it increased again by 0.49 and 0.31 respectively, giving average levels in the thirteenth week of 1.32 on cortisone and 1.29 on aspirin.

Very similar reversals were seen in all the other characteristics measured or observed. In Table VII they have already been shown for the functional capacity. It is, however, apparent that the two treatment groups have, on the whole, kept remarkably in step. They closely parallel one another in their immediate and favourable reaction to the first week of treatment; in the continuation of that reaction, but at a much slower rate, up to the observations made at week 8; in their unfavourable response to the cessation of treatment in week 13; and, finally, in their position at the end of the first year of the trial.

The haemoglobin levels and blood sedimentation rates have responded rather more favourably to cortisone than to aspirin. In all other respects there has been little to choose between the two agents. On each form of treatment joint tenderness is substantially reduced, on each form the disease is judged at the end of one year to be inactive, or only slightly active, in three-quarters of the patients, on each form two-fifths of the patients were regarded at the end of one year as capable of normal work and activity. As usual with cortisone treatment, certain more intangible differences have been observed. Some patients appear to experience a sense of well-being, and sometimes an almost excessive and inappropriate cheerfulness during therapy, followed by a swing to a mood of depression during the periods off treatment. On the other hand, the patients receiving aspirin tend to have changes in mood which are more in keeping with the increase and decrease in their symptoms. For practical purposes, however, there seems to have been surprisingly little to choose between cortisone and aspirin as adjuvants in the management of these 61 early cases of rheumatoid arthritis. The maintenance doses that were being employed at the end of the first year to produce these results are shown in Table VIII.

TABLE VIII.—*Daily Maintenance Doses being Administered at the End of the First Year (Before any Tapering-off)*

Cortisone (mg./day)	No. of Patients on Given Dose	Aspirin (g./day)	No. of Patients on Given Dose
125	2	6	8
100*	9	5	2
75†	7	4	13
62½	2	3	1
50	4	2	1
37½	1	1·7	1
25	1		
Total ..	26	Total	26
Nil (off treatment) ..	4	Nil (off treatment)	2
Mean value for those on treatment ..	80 mg.	Mean value for those on treatment ..	4·5 g.

* Including 1 at 105 mg. † Including 1 at 80 mg.

In the second year of the trial it is intended that treatment shall be continuous—unless the patient is in remission or is held to require no maintenance dose.

Summary

Sixty-one patients in the early stages of rheumatoid arthritis, and regarded as suitable for treatment with either cortisone or aspirin, have been allocated at random to treatment with one or other agent (cortisone 30 cases, aspirin 31 cases). Two comparable groups of these early cases were thus constructed and have now been treated and observed for one year. For most of the year treatment was "individualized" by the physician in charge of the patient at a level sufficient to restore maximal functional efficiency without producing serious side-effects.

Observations made one week, eight weeks, thirteen weeks, and approximately one year after the start of treatment reveal that the two groups have run a closely parallel course in nearly all the recorded characteristics —namely, joint tenderness, range of movement in the wrist, strength of grip, tests of dexterity of hand and foot, and clinical judgments of the activity of the disease and of the patient's functional capacity. The haemoglobin level and blood sedimentation rate were slightly more favourably influenced by cortisone, but in no other respect do the two groups differ materially.

On each form of treatment the disease was judged at the end of one year to be inactive, or only slightly active, in about three-quarters of the patients, and on each treatment some two-fifths of the patients were regarded as capable of normal work and activity. For practical purposes, therefore, there appears to have been surprisingly little to choose between cortisone and aspirin in the management of these 61 patients in the early stages of rheumatoid arthritis.

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THE ARTIFICIAL MENOPAUSE

WITH PARTICULAR REFERENCE TO THE OCCURRENCE OF SPINAL POROSIS

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Many states of ill-health have been attributed to the menopause, and it has been suggested that these manifest themselves more severely if the menopause is produced artificially. In addition to the disorders already recognized there has been added in recent years the occurrence of osteoporosis affecting mainly the spine and pelvis. Thus Albright and Reifenstein (1948) state that "a moderate degree of osteoporosis of the spine is almost physiological after the menopause: its degree increases as the time during which the post-menopausal state has existed increased." This statement implies that one should expect to encounter a larger number of cases of spinal porosis, possibly at an earlier age, in women who have been subjected to an artificial menopause.

It was with the idea of investigating this problem that the present inquiry was instituted, and an opportunity was taken to study other manifestations attributed to the menopause.

In discussing post-menopausal osteoporosis we are adhering to the definition of Albright and his associates presented in a series of recent publications. The term implies a condition in which there is no abnormality in either calcium or phosphorus metabolism, but in which there is a depression of osteoblastic activity, presumably due to hormone imbalance brought about by oestrogen lack; and the serum calcium, phosphorus, and alkaline phosphates are within normal limits, though there is a tendency for the serum phosphate to be slightly higher (Reifenstein, Kinsell, and Albright 1946).

Post-menopausal Osteoporosis: Clinical Investigation

Two groups of patients formed the basis of this investigation. The first group consisted of 94 women who had been subjected to an artificial menopause either by surgery or by radium at St. George's Hospital at least eighteen months prior to this study. For comparison a second group was studied; this consisted of 28 women who attended hospital because of backache and were found to have spinal porosis. All but two of these patients were seen at the Royal National Orthopaedic Hospital. Both groups were interviewed and clinically examined by one of us (J. R. N.). Particular attention was given to the following points: (1) radiological evidence of osteoporosis, (2) estimation of serum phosphate, (3) dietary history, (4) blood pressure, (5) changes in weight, (6) the incidence of hot flushes, and (7) changes in libido.

Radiological Evidence.—The radiological evidence of the early stages of osteoporosis of the spine is difficult of interpretation, and we were fortunate in having all the films assessed by the same radiologist. For convenience the abnormalities found have been divided into three grades: (1) A marked stencilling of the vertebral bodies with coarsening of bone trabeculation. (2) The above, together with swelling of the intervertebral disks, giving rise to biconcavity and the so-called codfish vertebrae. (3) The above with, in addition, crush fractures.

Group 1

In the first group of patients follow-up inquiries were sent to 150, but 56 could not be traced. Of the 94 patients who were interviewed and examined, 82 had had surgical removal of both ovaries and 12 had had the menopause induced by radium. The interval between operation and interview ranged from 18 months to 13 years. The age of the patients at the time of operation varied from 26 to 73 years, but the majority were in the fifth decade (56 patients) and the sixth decade (28 patients). Nineteen were spinsters, and of the remaining 75 who had been married 9 had never been pregnant.

Three of the 82 patients who had had surgical removal of the ovaries failed to have a radiological examination of the spine. Ten (12.6%) of the remaining 79 showed radiological evidence of osteoporosis. Only one of them complained of backache. Details of these 10 cases are:

Age at examination	49	51	55	56	58	59	61	69	69	76
Age at operation ..	43	48	42	50	55	56	58	67	65	73
Interval in years ..	6	3	13	6	3	3	3	2	4	3

Only 2 of the 12 patients who had been subjected to a radium menopause showed evidence of osteoporosis. They were aged 59 and 62 at the time of the examination, and 46 and 49 at operation, giving an interval of 13 years in both cases.

Thus of the 94 patients, 12 (12.7%) showed some radiological evidence of osteoporosis, and 3 of them were over 65 at the time of examination. Not one of these 12 patients showed a porosis which was of a greater severity than grade I, which can most certainly be regarded as physiological in the three patients over 65, and open to argument with regard to the remainder.

The average level of serum phosphate for the group which had undergone surgical menopause was 2.6 mg. per 100 ml. and for the 12 patients subjected to radium menopause it was 3 mg. per 100 ml. of serum.

All these patients were asked about their dietary habits, and no information was obtained indicating any marked deviation from normal.

In this series of patients the incidence of osteoporosis can be regarded as within the physiological range, and no significant abnormality in serum phosphate was observed.

Group 2

The second group, comprising 28 patients, all came to hospital with a specific complaint of pain in the back. Details are shown in Table I. The average age at examina-

TABLE I.—*Patients Treated for Post-menopausal Osteoporosis of Spine*

Case No.	Duration of Backache	Age at Onset	Age at Exam.	Age at Menopause	Years Between Menopause and Exam.	Married or Single	Parity		Grade of Porosis
							C.	Mis.	
1	6 months	43	43	41 (N)	2	M.	0	0	3
2	2 years	43	45	34 (A)	11	,,	0	0	3
3	2 ,,	47	49	47 (N)	2	,,	1	0	2
4	2 ,,	49	51	37 (N)	14	S.	0	0	3
5	2 ,,	49	51	46 (N)	5	M.	0	0	2
6	2 ,,	51	53	40 (A)	13	,,	1	0	3
7	6 months	53	53	23 (A)	30	,,	0	1	3
8	6 ,,	54	54	45 (A)	9	,,	0	0	3
9	15 ,,	57	58	52 (N)	6	,,	1	1	3
10	9 ,,	57	58	46 (N)	12	,,	0	0	2
11	8 ,,	57	58	45 (N)	13	S.	0	0	3
12	6 ,,	60	60	43 (N)	17	,,	0	0	3
13	6 ,,	62	62	30 (A)	32	M.	0	0	2
14	9 ,,	61	62	52 (N)	10	S.	0	0	2
15	6 years	58	64	45 (N)	19	M.	10	0	3
16	2 ,,	62	64	53 (N)	11	,,	3	0	3
17	2 ,,	63	65	45 (A)	20	S.	0	0	2
18	7 months	64	65	41 (A)	24	M.	0	0	2
19	6 ,,	65	65	39 (N)	26	,,	3	0	2
20	3 years	63	66	45 (N)	21	,,	1	0	3
21	1 year	69	70	50 (N)	20	,,	3	0	2
22	14 months	69	70	38 (N)	32	,,	3	0	3
23	4 years	66	70	52 (N)	18	,,	0	0	2
24	1 year	70	71	50 (N)	21	,,	0	0	3
25	1 ,,	71	72	30 (A)	42	,,	3	1	3
26	3 years	69	72	31 (A)	41	,,	1	0	3
27	2 ,,	70	72	45 (N)	27	,,	0	0	3
28	2 months	73	73	50 (N)	23	,,	2	0	3

N. = Natural. A. = Artificial. C. = Number of children. Mis. = Number of miscarriages.

tion and investigation of these patients was 61.6 years. Their individual ages ranged from 43 to 73. Nine patients were over 65, and 15 had had no pregnancies. Of these 28, 9 had been subjected to some form of pelvic surgery, with removal of either one or both ovaries. An accurate history of the surgical procedure was impossible to obtain in all cases.

Eighteen of these patients had grade 3 porosis and 10 had grade 2.

Of the 27 patients for whom serum phosphate figures were available the average was 3.6 mg. per 100 ml. This finding of an increase in the serum phosphate level is in agreement with the observations of Albright, Smith, and Richardson (1941).

The age of these women at the time of the menopause, whether artificial or natural, ranged from 23 to 53. The ages at the time of operation could be ascertained, but it must be understood that, particularly among the older women, the exact date of the menopause was difficult to obtain, but was probably accurate to within a year or two. The onset of symptoms after the menopause, whether artificial or natural, varied from 2 to 42 years. The average time of onset of symptoms in the 9 patients on whom an operation had been performed was 21.6 years from the time of operation. In the 19 patients on whom no operation was performed the average time of onset of symptoms from the date of their menopause was 15.2 years. We feel that this disparity is due to the small number of cases in this series.

Comment.—Albright, Smith, and Richardson (1941) gave clinical data about 42 patients with spinal osteoporosis, 40 women and 2 men. Because of the possibility of senescence being a factor no patient over the age of 65 was included. Of the 40 women in their series, 10 had been subjected to an artificial menopause. The average time of onset of symptoms in these 10 patients following the operation was 13.4 years, whilst in the remaining 27 (three women were excluded because of complicating thyrotoxicosis) the average time was 9½ years. The difference between these values was not regarded as being statistically significant.

Observations on Blood Pressure

A blood-pressure reading of over 150/90 was regarded as abnormal. In the first group of 94 patients 28 had a raised blood pressure; of these, 7 had a high blood pressure recorded prior to operation, and 20 (including 5 of the 7) gave a family history of severe cardiovascular disease in one or other parent. Thus 6 (6.3%) of the 94 patients had an unexplained rise of blood pressure, and the average age was 55.3 years.

Changes in Body Weight

In the first group of 94 patients, 54 stated that they had gained over 14 lb. (6.4 kg.) since the operation, 20 had gained less than 14 lb. (6.4 kg.), 20 noted no change in weight, and 5 had lost weight. This confirms the impression that, following an artificial menopause, a gain in weight is to be expected, though it does not invariably occur. In 26.5% of patients the weight remained unchanged or decreased. Bland-Sutton and Giles (1926) were of the opinion that complete removal of both ovaries "may cause obesity in a woman who has a tendency to form fat." There was a correlation between marked increase in weight and severe hot flushes, and vice versa, in 70% of patients. Whether there is any significance in this observation is uncertain.

Incidence and Duration of Hot Flushes

These were studied in the first group of patients. In Table II this series is analysed according to age groups and method of induction of the menopause; the results of other observers are included for comparison. Approximately 75% of patients complained of hot flushes after removal of both ovaries; this agrees with the investigations of other workers. The duration varied between 4 and 24 months. The younger the women were at the time of the menopause the greater was the increase in percentage. In the younger age groups the flushes were more severe, but the total duration tended to be shorter. It has been suggested that the flushes are worse after a radium-induced menopause; this contention is not supported by this small series, in which 66.6% developed this symptom. McLaren (1950) stated that 50% developed hot flushes. The incidence of hot flushes occurring in association with the natural menopause is obtained from two investigations into a larger series of women.

TABLE II.—*Incidence and Duration of Hot Flushes. Present and Previously Reported Series*

Information about Series Reported	Age Group at Menopause	No. of Patients	Total % Reporting Flushes	% of Severe Flushes	% Without Flushes	Average Duration
Present Series, Group 1:						
Removal of both ovaries	20–30	2	100	100	0	12 months
	30–40	8	74·4	62	25	6–12 months
	40–50	47	72·7	50	22·6	4–24 months
	50–60	25	32·0	24	52	6–24 months
Radium-induced menopause	40–50	9	66·6	55·5	33·3	Up to 24 months
	50–60	3	66·6	66·6	33·3	Up to 24 months
Natural and artificial menopause (Med. Women's Fed., 1933)	23–73	1,000	62·3	—	15·8	2–5 years up to 10 or 20
Natural menopause (McDowell and Paterson, 1940)	40–45	111	75	—	25	—
Removal of both ovaries (Bland-Sutton and Giles, 1926)	—	—	80	—	20	3–4 years up to 10 years
TeLinde and Darner (1928) (TeLinde and Darner quoted Cullen (1909), who gave same %)	—	—	74	—	26	—
Stacy (1930)	—	51	78	—	22	—
Sessums and Murphy (1932)	Under 36	36	80	73	20	7·2 months
Filler and Drezner (1944)	71% under 35	44	85	—	15	—
Richards (1951)	Under 45	42	98	—	—	—
Following radium menopause (McLaren, 1950)	—	—	50	—	—	Months or years

The Council of the Medical Women's Federation (1933) found that 62.3% of 1,000 women complained of hot flushes. The duration varied from 2 years up to 20 years. McDowell and Paterson (1940) found that 75% of 111 women between 40 and 45 complained of hot flushes.

It is interesting to note that about 20 to 25% of women do not complain of hot flushes after the artificial menopause. The reason for this, like the cause of the hot flush, has yet to be elucidated.

Changes in Libido

Alteration in libido following removal of the ovaries has long been studied. Battey (1876), writing about the "extirpation of the functionally active ovaries for the remedy of otherwise incurable diseases," was of the opinion that the aphrodisiac propensity was not annulled after the removal of the ovaries. Goodell (1879) was of the opinion that removal of the ovaries does not unsex a woman, and he quoted Koeberlé to the same effect.

Interrogation of the married patients in the first group showed that libido was decreased in 65%. These findings are further analysed in Table III with those of other workers for comparison.

A varying percentage of patients have decreased libido following removal of the ovaries; this is to be expected when the host of factors which influence libido are considered. Lewis and Jackson (1940) found that assessment was difficult because so many were frigid before operation.

The percentage tends to be higher in the younger age groups, though Filler and Drezner (1944), who studied 36 negresses in their series of 41 cases, did not confirm this, and

TABLE III.—*Change in Libido Following Artificial Menopause*

Series	Age Group	No. of Patients	Libido		
			De-creased %	Un-changed %	In-creased %
Present series, Group 1:					
Removal of both ovaries	20–30	1	100	—	—
	30–40	5	80	20	—
	40–50	32	62·5	34·3	3·1
	50–60	13	61·3	38·7	—
Radium-induced menopause	40–50	8	62·5	37·5	—
	50–60	1	—	100	—
Removal of both ovaries (Bland-Sutton and Giles, 1926)	—	—	32	68	—
TeLinde and Darner (1928)	—	52	40·4	53	5
	20–29	6	83·3	16·6	—
Lewis and Jackson (1940)	36–55	25	50	—	—
Filler and Drezner (1944)	71% Under 55	41	7	88	5
Koppen (1948)	—	50	30	—	—
Huffman (1950)	26–40	68	10·2	89·7	—
Richards (1951)	Under 45	33	60	—	6

Huffman (1950), by careful supervision, reported only a small percentage with decreased libido.

In all series there is a significant percentage in which the libido is unchanged after artificial menopause; this stresses the fact that the ovary is not essential for sexual libido and demonstrates the importance of complex factors, including upbringing, education, and marital relationships. Bland-Sutton and Giles (1926) stated that "facts are accumulating which tend to show that the ovaries are not the seat of the sexual passion . . . the complete removal of both ovaries is followed in adult women by *sterility* and persistent *amenorrhoea*, and these are the only two constant effects attributed to it."

Novak (1948) stated: "In the human being the ovary has very little to do with libido, the sex sense . . . in the human female; the seat of libido is in the psyche with certain auxiliary erogenous zones such as the vagina, the clitoris, and the mammary gland. The ovaries in themselves are not essential at all to sex gratification."

These points have been further studied in pre- and post-operative discussions with patients not included in this series. Reassurance and correction of preconceived and erroneous beliefs has permitted return of libido, and it has been established beyond question that a full orgasm can subsequently be obtained. Adequate briefing should be considered as essential in the management of such patients.

Conclusions

There was no evidence that osteoporosis of significant degree was precipitated by an artificial menopause, or that, in patients with established osteoporosis, it occurred at an earlier age following an artificial menopause.

The occurrence of post-menopausal osteoporosis is unpredictable; the time of its onset or severity cannot be related to the age at which the menopause—natural or artificial—occurs, or to the number or frequency of pregnancies. The tendency for the serum phosphate level to be raised in patients with fully developed porosis is confirmed.

There was no evidence that hypertension was attributable to the artificial menopause. The hereditary factor was clearly demonstrated by the high proportion of those hypertensive patients who gave a family history of severe cardiovascular conditions in one or other parent.

An increase in weight occurs in most patients, but there was no increase or even a decrease in weight in 26.5%.

Hot flushes occurred in approximately 75% of patients. The duration varied between 4 and 24 months. The incidence is higher and the duration tends to be shorter in the younger age groups. There was no significant difference between patients who had had a surgical menopause and those with a radium menopause. The incidence and duration are similar to those following the natural menopause in comparable age groups.

After an artificial menopause libido was decreased in approximately 65% of patients. The fact that the ovary is not essential for the maintenance of the libido is shown by the percentage of patients who were unaffected.

This investigation emphasizes that the only two constant effects of removal of the ovaries are amenorrhoea and sterility.

Summary

The occurrence of post-menopausal osteoporosis is discussed. The incidence of osteoporosis in 94 patients following artificial menopause is analysed. A group of 28 patients with definite osteoporosis is investigated in relation to the lapse of time after a natural or artificial menopause.

The serum phosphate levels in both groups of patients are given.

The incidence of unexplained raised blood pressure after an artificial menopause is recorded and discussed. The change in weight following artificial menopause is recorded.

The incidence and duration of hot flushes in 94 patients who had an artificial menopause are detailed.

The change in libido in patients after induced menopause is discussed.

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Turning down the $10,300,000 recommended by its committee on programme and budget, the Seventh World Health Assembly adopted a regular budget of $9,500,000 for 1955, an increase of $1,000,000 over last year's. This decision was taken by a vote of 28 to 24, with 7 abstentions. The United States proposal for an even smaller budget of $8,607,000 was rejected by 35 votes to 21, with 6 abstentions. The Indian proposal for a budget of $9,900,000 did not come to a vote, and the ceiling of $9,500,000 adopted by the Health Assembly came from a proposal of the United Kingdom. By unanimous vote the Federation of Rhodesia and Nyasaland, established eight months ago, was admitted to Associate Membership in the World Health Organization. Other W.H.O. Associate Members are Tunisia and Morocco. The Assembly has also recommended that the next Assembly consider methods of assessing only active members for the regular effective budget, and invited those States which have not been actively participating in the work of the organization to resume participation at the earliest date.

VARICOCELE IN GROUPS OF FERTILE AND SUBFERTILE MALES*

BY

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In the course of a study entailing physical examination and semen analyses in groups of fertile and subfertile men I have noted a higher incidence of varicocele in men with poor quality semen. Varicocele is a relatively common condition mainly affecting young men (Skinner, 1941; Turner, 1943; Boyd, 1947; Aird, 1949), and Bailey and Love (1941) quote an incidence of 5 to 10% in men between the ages of puberty and 35. Marriage and the passage of years usually bring about a diminution in the size of the varicocele (Skinner, 1941; Turner, 1943; Aird, 1949), so that the incidence is likely to decrease as age increases.

In this country the traditional attitude adopted by surgeons to varicocele is given by Professor Charles Wells (1948): "In civilian practice very little importance is attached to this condition. On the assumption that the condition is little more than an exaggeration of the normal with an added neurosis, reassurance and local support with a suspensory bandage may safely be advocated as the treatment in most cases."

Wells (1953, personal communication) has emphasized the very real danger of damage to the testis caused by active surgical treatment. Douglas (1921) and Campbell (1928) have also drawn attention to the inadvisability of operative treatment. Douglas followed up 106 cases of varicocele treated by operation and found that 41 of the men had hydrocele and 4 had atrophy of the testis. Haemorrhage, hydrocele, infection, epididymitis, and loss of a functioning testis by atrophy are possible complications of operative treatment (Douglas, 1921).

The investigation reported in this paper was begun in the Gynaecological Department of the Aberdeen Royal Infirmary in 1947 and continued in the Department of Obstetrics and Gynaecology in the University of Durham. The diagnosis of varicocele is a matter of opinion, but in this investigation there was one observer, and the criteria for diagnosis remained constant. Only in those cases in which there was palpable and visible enlargement of the pampiniform plexus was a diagnosis of varicocele made.

Clinical Material

The incidence of varicocele in the following groups is reported.

Group I.—This comprised 52 men of high fertility. All had had five or more children and their semen was of excellent quality. The spermatozoon counts ranged from 64,000,000 to 250,000,000 per ml. In each case the man's wife had been delivered recently either in the Aberdeen Maternity Hospital or in the Princess Mary Maternity Hospital, Newcastle-upon-Tyne.

Group II.—This consisted of 48 men who had had two, three, or four children. Their spermatozoon counts ranged from 37,000,000 to 259,000,000 per ml. Their wives had been delivered recently either in the Aberdeen Maternity Hospital or in the Princess Mary Maternity Hospital.

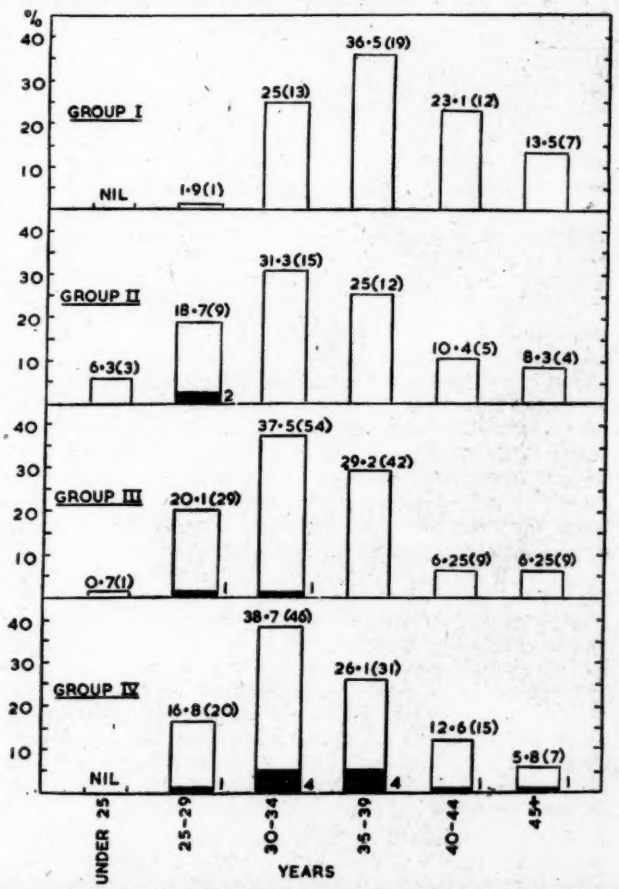
Group III.—This comprised 144 men examined at subfertility clinics in Aberdeen or Newcastle-upon-Tyne. Their wives had had no children, but these men were found to have good quality semen. In each case the count was above 75,000,000 per ml.

Group IV.—This consisted of 119 men examined at subfertility clinics in Aberdeen or Newcastle-upon-Tyne. Their wives had had no children, and in each case the spermatozoon count was below 50,000,000 per ml.

For the purpose of this paper spermatozoon density has been used as the criterion of semen quality. It is generally agreed that as the spermatozoon count per ml. falls other defects in semen quality increase (Hammen, 1944; MacLeod and Hotchkiss, 1946; Simmons, 1947; Tyler, 1951).

A standard method of collecting semen specimens was employed throughout the study. In each case a period of abstinence of at least four days was stipulated, and ejaculation took place into a clean glass jar. The specimens were analysed within three hours of production. One sample was examined from each of the fertile men in Groups I and II and from the 144 men attending the subfertility clinics who were found to have spermatozoon counts above 75,000,000 per ml.

Most of the men in Group IV had at least two analyses made, and in some of them had repeated analyses over periods of several months. The average figure has been calculated for each man in this group.



Percentage of patients in the groups studied. The actual number of patients in the various groups is given in parentheses and the shaded areas at the bottom of certain columns, with figures alongside, show the actual number of cases of varicocele and how they were distributed throughout the groups.

Results

Fertile Men

Group I.—No case of varicocele was discovered in these highly fertile men.

Group II.—There were two cases of varicocele in this group. The first was in a man aged 27 who had been

*Based on a paper delivered to the Society for the Study of Fertility, Liverpool, June, 1953.

married three years and had had two children. No abnormality was detected in the testes, and the spermatozoon count was 129,000,000 per ml. The other case was that of a man aged 29 who had been married four years and had had two children. The testes appeared normal and the spermatozoon count was 68,000,000 per ml.

Men Examined at Subfertility Clinics

Group III.—Among these men with good quality semen two were found to have varicocele (1.4%). One was a man aged 32 who had been married two and a half years and whose wife had failed to conceive. The testes were normal in size and consistence, and the spermatozoon count was 78,000,000 per ml. The other was a man aged 27 who had been married three years and whose wife had failed to conceive. The testes were normal in size and consistence, and the spermatozoon count was 94,000,000 per ml.

Group IV.—Among these 119 men with poor quality semen 11 were found to have varicocele (9.2%). Details are given in the Table.

11 *Cases of Varicocele Among* 119 *Men with Poor Quality Semen*

Case	Age	Occupation	No. of Years Married	Site of Varicocele	Testes	Average Spermatozoon Count per ml.
1	28	Barman	5	Left	Normal	15,000,000
2	31	Electrician	5	,,	,,	43,000,000
3	32	Bus driver	6	,,	,,	33,000,000
4	34	Schoolmaster	10	,,	Both small	10,500,000
5	34	Bus driver	8	,,	Normal	38,000,000
6	35	Motor mechanic	9	,,	,,	13,500,000
7	36	Baker	12	,,	,,	9,000,000
8	36	Fisherman	11	,,	,,	35,000,000
9	37	Cobbler	6	,,	Left small and soft	16,000,000
10	40	Schoolmaster	6	,,	Left soft	10,000,000
11	45	Commercial traveller	2	,,	Normal	17,000,000

Discussion

Hotchkiss (1945), a leading authority on male fertility, points out that there is no agreement on the exact relationship which varicocele bears to infertility.

A number of authors record the finding of cases of varicocele among men examined at subfertility clinics, but details of age, duration of marriage, etc., are not given. Hammen (1944), for example, reports the finding of varicocele, in varying degrees, in 11.9% of 291 patients referred to his subfertility clinic in the Kommune Hospital, Copenhagen—not all of these 291 patients were subfertile. He found that 92% of the patients with varicocele had spermatozoon counts below 60,000,000 per ml. Tyler (1951) found a "significant" degree of varicocele in 6 out of 82 men with spermatozoon counts between 20,000,000 and 59,000,000 per ml.—an incidence of 7.3%; among 53 men with counts above 60,000,000 per ml. the incidence was 3.8%. Jeffcoate (1946) found the condition present in nine men whose wives had been referred to him on account of childlessness. Seven of these men had poor quality semen.

On the other hand, Michelson and Michelson (1947) examined 519 men with poor quality semen and discussed the aetiological factors which were found, but the occurrence of varicocele in these men is not mentioned.

A number of interesting features are shown in the results of the present study. In men with poor quality semen (Group IV) the incidence of varicocele was found to be 9.2%, as compared with 2% among fertile men (Groups I and II) and 1.4% among men who, although their wives had failed to conceive, were found to have good quality semen (Group III).

It was stated above that the condition tends to affect young men, and it was therefore important to analyse the groups by age—the results are shown in the Chart. The highly fertile men in Group I were on the average a few years older than the men in the other groups—73% were 35 or over. There was, however, little difference in age between the men in Groups II, III, and IV, the number of men of 35 and over being 44%, 42%, and 45% respectively. There is therefore the possibility that the greater average age of the highly fertile men in Group I may have been in part responsible for the absence of varicocele in these men. On the other hand, the men in Groups II, III, and IV are comparable so far as age is concerned, yet varicocele occurred almost seven times more frequently in the men with poor quality semen (Group IV). Although the number of cases of varicocele is small there is a significant increase in incidence in the subfertile group of men—the probability is less than 0.01.

One further point in regard to age is of some interest. Varicocele was found four times in men with good quality semen (Groups I, II, and III)—all were young men, the oldest being 32. Of the 11 men with poor quality semen who were found to have varicocele (Group IV) only one was under 30 and six were 35 or older (see Table). This suggests that a varicocele which persists beyond the age of 30 years is more liable to be associated with subfertility, and, conversely, one which disappears before the age of 30 is not likely to interfere with fertility. This is only a suggestion and may not be true, as it is equally possible that a number of cases of unexplained atrophy and softening of the testes among subfertile men may in fact be legacies from varicoceles which have regressed.

Although it is beyond the scope of this paper to discuss the aetiology of varicocele, I could find no evidence to support the view that late marriage is an important cause of the condition. The Table shows the age of marriage of the 11 men with varicocele in Group IV: most of them had married at an early age and had been married for several years.

The Table also shows the predilection of varicocele for the left side; this tendency is widely recognized and has been reported in the literature by many workers. Softening and even atrophy of the left testis is not unusual, and was noted in 3 of the 11 cases of varicocele occurring in the subfertile men. Hammen (1944) found diminution in size or consistency of the testis on the same side in 35.3% of his patients with varicocele. It is difficult to explain why a lesion which is generally one-sided should affect spermatogenesis in the other testis. A possible explanation is a slight but prolonged alteration in temperature within the scrotum, affecting both testes.

Summary and Conclusions

This study points to an important association between varicocele and subfertility, for the incidence of the condition is much higher in men with poor quality semen. The more frequent occurrence in subfertile than in fertile men cannot be explained entirely by their being in different age groups.

There is evidence to support the view that a varicocele persisting beyond the age of 30 is particularly apt to be associated with poor quality semen, but this study gives no information of the proportion of varicoceles that do continue beyond the age of 30.

The purpose of this paper is not to plead for more active treatment (indeed, attention has been drawn to the dangers of active surgical treatment), but rather to challenge the traditional attitude that varicocele is an innocuous condition and to stress the need for more extensive investigation into the natural history of varicocele and the effect which it may have upon fertility.

I am most grateful to Professor Harvey Evers and Mr. Frank Stabler for their encouragement and helpful criticism. The statistical significance of the increased incidence of varicocele in the subfertile men was confirmed by Mr. Hubert Campbell, statistical assistant in industrial health, University of Durham.

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THE AURICULO-TEMPORAL SYNDROME

BY

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In 1897 Parkes Weber demonstrated the strange case of a youth who, following a suppurating lesion in the region of his left parotid gland, sweated on that side of his face when he ate food. Accompanying this there was a flushing on the same side of his face. Because the area involved corresponds to the cutaneous distribution of the auriculo-temporal nerve this condition became known as the auriculo-temporal syndrome. Lucie Frey described it again in 1923, and because of her work on the subject it is also known as Frey's syndrome.

The auriculo-temporal syndrome consists of redness and sweating over the temporal and pre-auricular areas evoked by eating. It is a sequel of penetrating wounds, surgical incisions, or suppuration in the region of the parotid gland. The redness and sweating are not synchronous in appearance, the vasodilatation occurring first. Nor are they conterminous in distribution. There may be pain during eating, and sensory changes in the form of diminished or increased sensation in the same area are commonly present.

Case Report

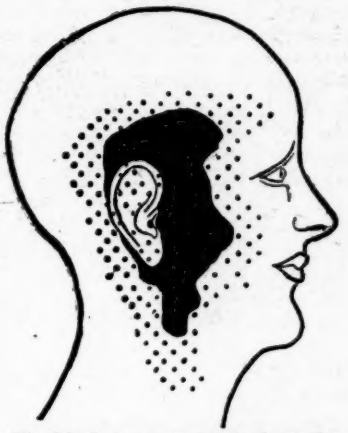
A woman of 36 had the superficial part of her right parotid gland and adjacent fibrous tissue excised for chronic parotitis. From 2 years of age she had suffered from repeated attacks of painful inflammation, and periglandular fibrosis had produced a partial false ankylosis of the right temporo-mandibular joint. The operation prevented further attacks of parotitis and she was enabled to open her mouth enough to take food normally. Six months later it was noticed that during a meal sweat appeared on the side of her face and trickled down her cheek.

Examination

On examination a 4-in. (10-cm.) scar was seen running parallel to, behind, and below the right ramus, angle, and body of the mandible. Skin sensation was normal. The parotid gland was impalpable, and the orifice of Stensen's duct appeared normal, and saliva issued from it. When the patient was given a caramel to eat the skin on the affected side of the face became red. The hyperaemia extended over the forehead, temple, cheek, and ear. Within a minute, pinpoints of sweat appeared over a less extensive area (see Fig.). Within five minutes the sweat had accumulated into drops large enough to run down the cheek. When she stopped eating the sweating ceased, the hyperaemia faded, and the skin returned to normal.

Anatomy and Aetiology

It is necessary to consider the anatomy, so far as it is known, in order to appreciate the theories that have been produced to explain the mechanism. Secretory parasympathetic fibres from the glossopharyngeal nerve pass to the auriculo - temporal nerve, providing the parotid gland with secreto-motor fibres. The sweat glands of the face are innervated by the sympathetic outflow, the post-ganglionic fibres of which are believed by Wilson (1936) to be distributed with the peripheral branches of the trigeminal nerve. Sweating of the face in response to heat is mediated by sympathetic pathways, for destruction of the cervical sympathetic chain reduces heat sweating (Guttmann, 1940). List and Peet (1938) suggest that there is parasympathetic innervation of sweat glands of the face. Wilson (1936) concluded that such fibres join the trigeminal nerve at some point distal to the sensory root. There is no evidence to suggest that they play any part in sweating under normal physiological conditions.



The black area represents the region of sweating. The stippled area represents the region of hyperaemia.

The auriculo-temporal syndrome occurs most often as as sequel of suppurative parotitis, which is so severe as either to rupture spontaneously or to require surgical incision and drainage (Parkes Weber, 1897; List and Peet, 1938; Freedberg *et al.*, 1948; Pfeffer and Gellis, 1951). Trioumphoff (1926) reported 14 cases having an antecedent history of suppurative parotitis and mainly secondary to typhoid or typhus fevers. Frey's case followed a gunshot wound which caused a secondary parotitis. Cases have been reported following excision of parotid tumours, and it has been described following mumps and in cases of syringomyelia (Kaminsky, 1929; Wilson 1936).

Mechanism

The hyperaemia and sweating are a reflex response, the afferent component of which is stimulated by taste. It appears that the disorder lies in the efferent arc which involves nerve fibres in the region of the auriculo-temporal nerve.

It has been suggested that scar tissue involves and anchors autonomic fibres which are subjected to pressure when the parotid gland distends, as it does when food is tasted.

Those cases in which the syndrome occurs promptly after a salivary fistula closes support this theory. Needles (1936) reported a case of temporary parotid fistula complicating the excision of a parotid tumour. The appearance of the auriculo-temporal syndrome coincided with the closure of the fistula. Needles referred to a case of bilateral parotitis. One side had a fistula and the other none. The auriculo-temporal syndrome occurred only on the side where there was no fistula. However, the phenomenon may occur when the parotid is either atrophied or functionless, and is not produced when pressure is exerted in the region of the scar.

Frey considered that the reflex was essentially a normal one, but that it had been accentuated through injury to the

auriculo-temporal nerve with subsequent irritation of vasodilator fibres in the cicatrix of the sclerotic parotid gland. In that way she incriminated scar tissue.

Another hypothesis is that it is due to faulty regeneration of parotid secretory fibres (Thomas, 1927; Ford and Woodhall, 1938).

Since one cholinergic fibre can replace another (Dale, 1935), a fibre originally destined for salivary glands may communicate with a sympathetic fibre passing to the skin. In that way a stimulus which would normally produce salivation evokes sweating. The frequently associated evidence of nerve injury supports this view. This includes abnormalities of skin sensation, decreased sweating in response to heat, pain, and facial palsy which is either transient or permanent.

The time interval that occurs between the injury and the appearance of the syndrome also supports this hypothesis. Time must be allowed for Wallerian degeneration and subsequent regeneration to take place. This theory fails to explain those cases in which the latent period is only of a few days' duration. Furthermore, one would expect the sudomotor fibres of the auriculo-temporal nerve, coming from the cervical sympathetic, to produce vasoconstriction and pallor and not the reverse when they are stimulated.

Freedberg *et al.* (1948) offer the explanation that the auriculo-temporal syndrome represents a response of denervated and hypersensitive sweat glands to previously unapparent cranial sudomotor impulses.

Hypersensitivity of afferent structures following denervation is an accepted physiological finding in both cholinergic and adrenergic nerves. It is a logical expectation that hypersensitivity of the sweat glands of the face may follow division of sympathetic fibres in the auriculo-temporal nerve. Freedberg *et al.* (1948) and Langenskiöld (1946) demonstrated this sensitivity.

Haxton's (1948) observation that sympathetic block in the upper thorax stops the response suggests that acetylcholine comes from intact nerve endings.

From the above findings it becomes apparent that the mechanism of the auriculo-temporal syndrome is not fully explained.

Allied Conditions

There are other conditions which at least superficially resemble the auriculo-temporal syndrome. The slight symmetrical sweating that occurs on the faces of normal individuals when they eat spicy food is accepted as a normal reflex. Sometimes this reflex is exaggerated and the sweating excessive. Its relation to the auriculo-temporal gustatory sweating is hypothetical but suggestive. Pfeffer and Gellis (1951) refer to Mellenkoff's case of an infant with a transient phase of sweating from a small area in the region of one tibial tubercle when milk was taken.

The syndrome of "crocodile tears," which consists of lacrimation occurring as a reflex response to eating, resembles the auriculo-temporal syndrome. It follows facial palsy, usually with the site of lesion in the region of the geniculate ganglion. Another condition which resembles the auriculo-temporal syndrome was reported by Uprus *et al.* (1934). Their patient had previously had cervical glands excised. Gustatory sweating subsequently developed in the submandibular region on the same side as the operation.

Prognosis and Treatment

The hyperaemia and sweating may continue for the remainder of the patient's life, but a diminution of symptoms sometimes occurs (Payne, 1940).

Since the auriculo-temporal syndrome is benign and non-progressive the patient can be reassured. If the discomfort warrants treatment the auriculo-temporal nerve may be divided surgically, but there are few records of this being done. Alcohol injection of the nerve is to be avoided because of possible injury to the facial nerve, and the value of radiotherapy is doubtful.

Summary

A case of the auriculo-temporal syndrome is reported.
The anatomy is considered.
Aetiology is discussed.
Theories of explanation are reviewed.
Reference is made to allied conditions.
Prognosis and treatment are described.

I wish to thank Mr. J. A. Martinez for his permission to report this case.

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RADIO-IODINE MEASUREMENTS OF THYROID FUNCTION DURING AND AFTER P.A.S. TREATMENT OF TUBERCULOSIS

BY

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Over the past three years there have been reported nine cases of hypothyroidism with goitre occurring during para-amino salicylic acid (P.A.S.) treatment (Bergqvist and Maré, 1951, 1952; Clausen and Kjerulf-Jensen, 1951; Komrower, 1951; Librach, 1952; Davies and Galbraith, 1953). As many thousands of patients have received this treatment this seems a small incidence which may have depended on some special susceptibility in these few patients. Others have reported simple enlargement of the thyroid gland without signs of disordered thyroid function during P.A.S. treatment—that is, lesser antithyroid effects (Bergqvist and Maré, 1951, 1952; Hamilton, 1953); indeed, in some of the cases reported as goitre with myxoedema the evidence of thyroid deficiency has been slight. Because of these reports we have endeavoured to assess whether doses of P.A.S. commonly used clinically entail much risk to thyroid function. Radio-iodine tests of thyroid uptake have therefore been carried out on an un-

selected* series of 30 patients at the conclusion of their period of P.A.S. treatment; one test being given just before and the other four to seven days after the drug was stopped. The difference between the pair of tests should indicate whether this P.A.S. dosage had influenced thyroid uptake of iodide; and an excessive thyroid uptake should be seen on the second test when any hyperplasia and iodine deficiency had been induced by the period of P.A.S. administration. In addition, by an *in vitro* test, one of us (M. H.) has compared the antithyroid potency of P.A.S. with that of 2-thiouracil.

Like other amino-benzene compounds (Astwood *et al.*, 1945), P.A.S. might be expected to be an antithyroid drug interfering with the normal iodination of the thyroid hormone, provided that P.A.S. entered the thyroid gland. This action is indicated by our *in vitro* test results and animal experiments (Kjerulf-Jensen and Wolffbrandt, 1951), but its potency in the dosage used clinically cannot be predicted from its formula nor from the *in vitro* measurements, which take no account of its entry into the thyroid gland. Horn and Bogsch (1950) observed a retardation of radio-iodine uptake during P.A.S. administration in one patient, and Hanngren (1952) found an inhibition of radio-iodine uptake for four hours after an intravenous dose of 10.5 g. of P.A.S. in another patient. Davies and Galbraith (1953) found an increased uptake of iodine in their patient after withdrawal of P.A.S., suggesting that some hyperplasia had been introduced. Hamilton (1953) noted that a goitre which developed during P.A.S. treatment decreased with thyroid administration, suggesting that its development had depended on the drug's antithyroid action. Sutherland (1953), in the United States of America, registered maximum retardation of radio-iodine uptake after four to six weeks of P.A.S. therapy. He also states that iodine uptake returns to normal one to two weeks after cessation of treatment. No cases of goitre were reported in this series, but it is not stated whether any patient was tested after prolonged P.A.S. administration.

Method

Unselected patients available for assessment at the conclusion of their period of treatment were each given two tests—one just before and the other at four to seven days after stopping the drug. Most patients had had approximately three months' continuous chemotherapy, and some had had the drug for a longer period; the dosage of P.A.S. had mostly been 20 g. daily, but other drugs had also been given to most of the patients. Details of the dosage of P.A.S. and associated drugs are given in Table IV. The test used was the urinary excretion of radio-iodine as described by Fraser *et al.* (1953); following the radio-iodine dose the urinary excretion was measured in three periods, 0–8, 8–24, and 24–48 hours after the dose. The excretion in 8–24 hours offers an inverse index of thyroid uptake. Since the P.A.S. level might have fluctuated during the period of the first test, the 0–48 hour excretion has also been used to provide a similar index—its modifiability by abnormal renal function should not matter with these patients, and its reflection of thyroid uptake would not be invalidated by any fluctuation in P.A.S. level during the first test.

The *in vitro* method used to assess antithyroid potency was that described by Pitney and Fraser in 1953. It measures the inhibition of the peroxide-iodination of protein by various concentrations of a drug, in a test in which the peroxide is provided by added milk enzyme powder and substrate. The antithyroid action of the drug is measured by the extent to which various concentrations of the drug inhibit the iodination of protein, and the data thus obtained have been referred to those obtained with 2-thiouracil for comparison.

*After the first cases were tested special search was made for patients given the drug for long periods; the cases were otherwise unselected.

Results

The results of the radio-iodine tests on the patients are summarized in Table I, and given in fuller detail in Table IV. The tests on the patients during P.A.S. administration are not clearly abnormal, but show more excretion of radio-iodine than do those after its withdrawal (Table I). The

TABLE I.—*Radio-iodine Test Results on Patients During and After Stopping P.A.S.*

Group	No. of Patients	Urinary Excretion of I^{131} (As Percentage of Administered Dose)			
		In 8–24 Hours		In 0–48 Hours	
		Mean±S.E.	S.D. (Range)	Mean±S.E.	S.D. (Range)
(*a*) Normals ..	32	13·6±0·65	3·7 (7–20)	55·8±1·54	8·7 (35–70)
Tuberculous patients:					
(*b*) While on P.A.S. for 3 months or more	30	19·9±1·95	10·7 (2·5–42·5)	55·3±2·96	16·2 (22·1–91·8)
(*c*) 4–7 days after stopping P.A.S.	30	8·8±0·93	5·1 (0·9–20·2)	33·2±1·88	10·3 (14·9–57·6)
Difference (*b*)–(*c*)		11·1±2·16		22·1±3·41	
Difference (*a*)–(*c*)		4·8±1·14		22·6±2·43	

The tests after cessation of the P.A.S. show more thyroid uptake than those during the drug administration and also than those of the normal patients—the excretions in either period are significantly higher.

8–24 hour excretion is high, but the 0–48 hour excretion is normal; clearly this dosage of P.A.S. had some antithyroid effect. Evidently the thyroid uptake of radio-iodine during P.A.S. administration is slowed but ultimately occurs to an approximately normal extent. Probably the slight compensatory thyroid hyperplasia induced over the previous months of P.A.S. administration is usually nearly enough to balance the weak antithyroid effect produced by the usual dosage of P.A.S.

As a group the tests on the patients after withdrawal of P.A.S. show less radio-iodine excretion in both periods than those of a normal group (Table I)—that is, there is a tendency to increased thyroid uptake of iodide after P.A.S. withdrawal, indicating some depletion of the thyroid hormone store during the previous drug therapy. These tests after withdrawal tend to show more abnormality when P.A.S. treatment has been more prolonged, particularly when it has exceeded six months (Table II). The increase of thyroid uptake is, however, usually slight, for, while the mean excretions for the groups are abnormal, few individual excretions are beyond the normal range, except when the drug has been given for over six months. Apparently slight compensatory thyroid hyperplasia had occurred during the previous months of P.A.S. administration, and usually it is only after more than six months of drug administration that much exhaustion of the thyroid hormone store is discernible. Probably the patients varied in their susceptibility to the drug, for among those given it for less than six months are several with one or both tests normal; and the differences between individual results (see Table IV) are greater than those between groupings according to the total duration of P.A.S. therapy.

Of the 11 patients given P.A.S. for over six months, 10 were found to have an obviously avid uptake of radio-iodide on P.A.S. withdrawal (Table II), and four were noted to have developed a small goitre of 40–50 g., first noticed 6½ months (Cases 29 and 30) and 8 months (Cases 27 and 28) after starting the drug. None showed any myxoedematous features. After the tests reported above, the first two patients (Cases 29 and 30) were given potassium iodide, 10 mg. daily for one week, and when seen one month later, while still off P.A.S., the radio-iodine uptake

TABLE II.—*Radio-iodine Tests After Withdrawal of P.A.S.*

Duration of P.A.S. Therapy (at 20 g./Day)	No.	Mean Urinary Excretion of I^{131} as % of Dose	
		In 8–24 Hours	In 0–48 Hours
Under 3 months* ..	8	10·7	39·2
3 months	8	11·5	37·1
3–4 ,, ...	3	10·2	33·4
6–10 ,, †	11	4·3	26·0
(Normal group) ..	(32)	(13·6)	(55·8)

* Includes two cases receiving 10 g. P.A.S. daily for three months.
† On P.A.S. 20 g. daily for three months, then 15 g. daily.

had become normal, and the thyroid enlargement had subsided. Neither had previously noted a goitre; the third and fourth patients were not retested after iodide, but one had a family history of goitre and may have had some goitre before his treatment.

TABLE III.—*In vitro Measurement of the Antithyroid Potency of P.A.S. and Isoniazid Compared with that of 2-Thiouracil*

Drug	Antithyroid Potency (Relative to 2-Thiouracil)	
	For 50% Effect*	Speed of Increase with Rising Concentration†
2-Thiouracil	(1)	(1)
P.A.S.	(0·085)	(0·02)
Isoniazid	(0·025)	(0·18)

* Potency for 50% inhibition equals reciprocal of that molar concentration of the drug which gives 50% inhibition on enzymic iodination test; for this the molar concentration is expressed as equivalents of the iodide present in the test.
†Speed of increase of antithyroid potency with rising concentration $= \frac{\text{molar concentration for 10\% inhibition}}{\text{molar concentration for 90\% inhibition}}$ on same enzymic iodination test.

Table III shows the results of the *in vitro* measurements of the antithyroid potency of P.A.S. and also of isoniazid expressed relative to the values found for 2-thiouracil. Both drugs appear to be weakly antithyroid, showing less than one-tenth of the potency of 2-thiouracil, and isoniazid about one-third the potency of P.A.S. Their antithyroid potency also increases much more slowly with rising concentration than does that of 2-thiouracil. These tests take no account of the degree to which the drugs can enter the thyroid, but are in conformity with the clinical findings that these are very weak antithyroid drugs.

Summary and Conclusions

Tests on 30 patients before and after withdrawal of P.A.S. treatment showed that the drug causes a slight interference with the uptake of iodine by the thyroid; during less than six months' administration this seems usually to be adequately compensated by slight thyroid hyperplasia. *In vitro* testing of antithyroid potency showed P.A.S. to be a weak antithyroid drug, and isoniazid to be even weaker. Except possibly in occasional patients exceptionally susceptible to the drug, and in those given P.A.S. for over six months, this effect probably has no clinical importance.

When the drug is given for over six months at a dose of about 20 g. a day thyroid function may be affected, 10 out of 11 patients having shown on withdrawal of the drug an avid iodine uptake indicating previous iodine depletion, and 4 out of the 11 having noticed the development of a goitre. In two of these patients these abnormalities were shown to be correctable by iodide administration. We suggest that when P.A.S. is to be given for over six months, a weekly dose of iodide should be given to avoid these thyroid effects—for example, a weekly potassium iodide pill (¼ gr., or 20 mg.).

We wish to thank the sisters and nurses for their help in the collection of specimens, and Miss M. Magee for the radio-iodine estimations. Our thanks are also due to Drs. J. C. Hoyle, W. Oswald, A. L. Punch, F. H. Scadding, and F. H. Young for permission to carry out these tests on patients under their care.

TABLE IV.—*Individual Test Results*

Case No.	Age and Sex	Drug Dosage: P.A.S. Duration (Months)	P.A.S. Total (g.)	P.A.S. Daily (g.)	Other Drugs	Urinary Excretion of I^{131} (% of Administered Dose): On P.A.S. 8–24 Hrs.	On P.A.S. 0–48 Hrs.	Off P.A.S. 8–24 Hrs.	Off P.A.S. 0–48 Hrs.	Difference 8–24 Hrs.	Difference 0–48 Hrs.
6	41 M	2–3	860	20	S	35·5	49·8	17·7	57·6	−15·8	+7·8
13	24 F		900	10	H	22·1	57·4	7·9	30·8	−14·2	−26·6
20	38 F		900	10	H	22·0	63·6	9·6	49·0	−12·4	−14·6
8	29 F		1,120	20	S	23·7	84·4	16·2	54·7	−7·5	−29·7
1	31 F		1,680	20	S	26·3	60·8	13·2	25·8	−13·1	−35·0
4	26 F		1,680	20	S	28·9	62·7	10·5	32·8	−18·4	−29·9
3	42 M		1,720	20	S	22·6	45·5	10·2	32·6	−12·4	−12·9
7	29 F		1,720	20	S	11·6	39·5	6·8	30·0	−4·8	−9·5
5	45 F	3	1,800	20	S	23·0	59·9	10·2	36·6	−12·8	−23·3
11	28 F		1,800	20	S	27·3	62·4	10·8	28·3	−16·5	−34·1
12	30 M		1,800	20	H	23·6	80·7	5·4	36·8	−18·2	−43·9
14	28 M		1,800	20	S	12·0	44·4	14·3	44·3	+2·3	−0·1
15	22 M		1,800	20	S	19·2	44·7	10·8	36·4	−8·4	−8·3
16	53 M		1,800	20	S	25·8	66·3	20·2	52·2	−5·6	−14·1
17	17 F		1,800	20	S	11·8	43·3	16·8	29·0	+5·0	−14·3
19	21 F		1,800	20	S	20·8	58·7	3·2	33·2	−17·6	−25·5
10	43 F	3–4	1,920	20	S	42·5	63·0	6·5	30·5	−36·0	−32·5
9	24 F		2,070	20	S	33·8	91·8	13·9	37·7	−19·9	−54·1
2	33 M		2,380	20	S	20·3	46·6	10·2	32·0	−10·1	−14·6
29	42 F†	6–10	3,200	20+15‡	S	18·4	71·5	1·6	15·7	−16·8	−55·8
21	48 M		3,300	20+15‡	S+H	11·0	44·3	5·0	24·2	−6·0	−20·1
22*	20 F		3,500	20+15‡	S	3·9	21·2	13·7	39·7	+9·8	+18·5
30	25 M†		3,600	20+15‡	S	14·9	45·3	1·4	14·9	−13·5	−30·4
23	33 F		3,800	20+15‡	S	10·7	41·3	4·3	32·9	−6·4	−7·4
24	55 F		3,800	20+15‡	S	18·6	77·1	1·9	30·0	−16·7	−47·1
27	40 M†		3,900	20+15‡	S	14·9	62·0	4·2	18·2	−10·7	−43·8
26	30 F		4,000	20+15‡	S	18·6	59·0	7·1	32·2	−11·5	−27·6
28	30 M†		4,200	20+15‡	S	2·5	22·1	0·9	19·0	−1·6	−2·1
18	28 F		4,800	20+15‡	S+H	13·8	38·7	2·8	28·6	−11·0	−10·1
25	27 M		5,000	20+15‡	S	17·1	50·9	5·9	30·5	−1·5	−20·4

Normal range: 8–24 hours, 7–20%; 0–48 hours, 35–70%. S=Streptomycin 1 g. daily for 3 months; interrupted—i.e., 1 g. two or three times weekly. H=Isoniazid. 100 mg. b.d.
* It is suspected that the results on Case 22 may have been entered in the reversed order—but they have been entered here as recorded.
† Developed goitre.
‡ 20+15=P.A.S. 20 g. daily for 3 months, thereafter 15 g. daily.

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ASSAY OF PLASMA INSULIN ACTIVITY BY THE RAT-DIAPHRAGM METHOD

BY

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Bornstein (1950) described a method for the assay of insulin in human plasma which was based on the fall of blood sugar of alloxan-diabetic hypophysectomized adrenalectomized rats (A.D.H.A. rats). Subsequently Bornstein and his colleagues determined the insulin content of plasma from various types of diabetic by this method (Bornstein and Trewhella, 1951; Bornstein and Lawrence, 1951a, 1951b). The published results of these workers were of such interest as to merit further study.

A.D.H.A. rats prepared in this laboratory have proved to be too delicate and to possess too unstable a blood sugar to permit their use for accurate insulin assay. Groen *et al.* (1952) described a method for the detection and assay of insulin in human plasma which was based on the glucose uptake of the isolated normal rat diaphragm surviving *in vitro*; as was first shown by Gemmill (1940), this uptake is raised by the *in vitro* addition of insulin to the fluid in which the isolated diaphragm is suspended. This method has been critically investigated as a quantitative procedure for the assay of insulin and a modified procedure applied to the determination of the insulin activity of normal human plasma.

Methods

Animals.—The hemidiaphragms of normal male albino Wistar rats of 100–150 g. were used in these experiments. The animals were starved for 18 to 24 hours before use.

For the preparation of alloxan-diabetic hypophysectomized rats (A.D.H. rats) male albino Wistar rats of 170–220 g. were used. They were first of all hypophysectomized, and then, one week later, made diabetic by the intravenous administration of alloxan.

Insulin.—A single sample of crystalline insulin (Boots) of potency 23.2 units per mg. was used as standard in these experiments. Solutions of this were freshly prepared for each assay.

Human Subjects.—The different samples of plasma collected from human subjects are designated as random (collected without previous preparation of the subject) or fed (collected from subjects two and a half hours after the oral administration of 50 g. of glucose).

Chemical Analysis.—Blood glucose and the glucose content of the incubation fluid in the insulin assay was determined colorimetrically by the method of Somogyi (1945).

Procedure

For the qualitative detection of insulin activity in human plasma the glucose uptakes of rat hemidiaphragms suspended in buffer were compared with the glucose uptakes of rat hemidiaphragms suspended in buffer to which the plasma had been added.

For the quantitative assay of insulin activity in human plasma two methods have been used, the single standard method and a four-point assay.

In the single standard method, the absolute glucose uptake of rat diaphragm in the presence of plasma was compared with the absolute glucose uptake of rat diaphragm in the presence of a single standard dose of insulin (2 milliunits per ml.). In each assay (unless otherwise stated) four hemidiaphragms (from different rats) were used for the determination of the basal glucose uptake and six for the determinations of the glucose uptakes in the presence of plasma and of insulin respectively. A standard dose of insulin of 2 milliunits per ml. was chosen, since this gave results very similar to those yielded by normal human plasma under these conditions.

In four-point assays the glucose uptakes of rat hemidiaphragms in the presence of two dilutions of plasma (1:16 and 1:4) and two concentrations of insulin (0.5 and 2 milliunits per ml.) were simultaneously determined.

Experimental Procedure

The basal glucose uptake of the isolated rat diaphragm was determined in buffer (Gey and Gey, 1936) containing 2.5 mg. per ml. of glucose. The glucose uptake in the presence of insulin was determined in buffer-glucose containing the appropriate concentration of insulin. For the determination of the glucose uptake in the presence of plasma, buffer-plasma mixtures were prepared containing 2.5 mg. of glucose and 0.25 ml. of plasma in each ml. of mixture. In all cases the gas phase during incubation was 93% O_2, 7% CO_2.

In typical experiments, human blood was drawn from the antecubital vein by a dry sterile syringe. The blood was transferred to centrifuge cups containing a little heparin and the plasma separated by centrifugation. The plasma sugar was then determined, and after preparation of the buffer-plasma mixture 1-ml. samples of the incubation fluids were placed in the main compartments of Warburg manometer flasks. Normal rats were then killed by decapitation and their diaphragms removed, divided, and washed for exactly five minutes at room temperature in buffer-glucose (glucose concentration 2.5 mg. per ml.) previously saturated with 93% O_2, 7% CO_2. The hemidiaphragms were then lightly blotted, transferred to the manometer flasks, and incubated for three hours at 37° C. at a shake rate of 100 cycles a minute.

After incubation the flasks were removed from the bath, cooled, and 0.2 ml. of the fluid taken for glucose estimation. The hemidiaphragms were then blotted dry and weighed on a torsion balance.

Calculation of Results

The glucose uptake of the diaphragm was calculated as mg. glucose/g. wet wt. diaphragm/hour. The estimate of variance given in the tables is the standard error of the mean.

In single standard assays the insulin activity of the plasma was calculated from a log-dose (of insulin)/response curve previously determined, the standard dose of insulin incorporated in the assay being used to fix the position of this

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log-dose response curve. In this calculation the slope of the log-dose response curve was assumed to be constant. The limits of error (P=0.05) were calculated from previously determined regression data for crystalline insulin, since the variance in different assays did not differ significantly.

In four-point assays the insulin activity of the plasma and limits of error were calculated from the assay data by the usual means.

The insulin activity of the plasma is expressed as milliunits of insulin per ml. of plasma (1 milliunit is 10^{-3} unit).

Results

Response of Rat Diaphragm to Insulin Added In Vitro

Table I and Fig. 1 record the glucose uptake of rat diaphragm in the presence of different concentrations of insulin added *in vitro*. The results are the mean values of data collected on six separate occasions during a two-weeks period in September, 1953. Regression lines could be fitted to these data which did not depart significantly from linearity. Since the slopes of these regression lines did not differ significantly, they have been pooled to give a common slope. A cube-root transfer was chosen to minimize the effects of slight curvature noted at the extremes of insulin concentration.

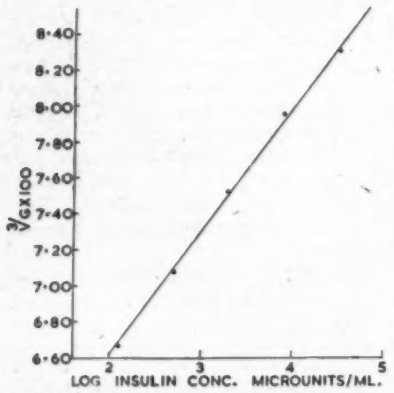

FIG. 1.—The effect of increasing concentrations of insulin upon the glucose utilization of the isolated rat diaphragm expressed as a log-dose (of insulin) response curve.

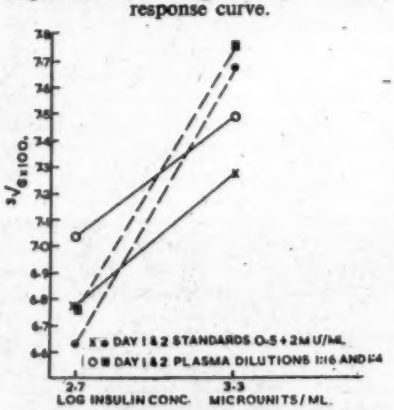

FIG. 2.—Four-point assays of the insulin activity of normal human plasma, by the rat-diaphragm method. Slopes of log-dose response curve for two concentrations of insulin and two dilutions of plasma. Insulin concentrations plotted as log dose (of insulin) in microunits per ml. Plasma insulin activity plotted as *insulin concentrations* in arbitrary units.

The lowest concentration of insulin producing significant stimulation of glucose uptake by the diaphragm was approximately 0.1 milliunit per ml. The slope (b) of the combined log-dose (of insulin) response curve was 0.6925 ± 0.033 (range of slopes 0.5966 ± 0.0838 to 0.8061 ± 0.0838) and the standard deviation of points about the regression line (s) was 0.25. The index of precision ($\lambda = s/b$) was 0.36. The slope of the log-dose (of insulin) response curve has been recently redetermined (January, 1954) and found to be 0.7081, in good agreement with the previous value.

The Insulin Activity of Normal Human Plasma

The method described has been applied to the determination of the insulin activity of plasma collected from normal human volunteers two and a half hours after the oral administration of 50 g. of glucose. The results of similar assays in acromegaly and hypopituitarism have been described in separate papers (Randle, 1954a, 1954b).

TABLE I.—*Effect of Increasing Concentrations of Insulin, Added In Vitro, Upon the Glucose Utilization of the Isolated Rat Diaphragm*

Insulin Concentration Microunits/ml. ($=10^{-6}$ unit)	Absolute Glucose Uptake	$\sqrt[3]{}$(Absolute Glucose uptake × 100)		No. of Hemi-diaphragms
		Observed	Calculated from Linear Regression	
0	2·32±0·05	—	—	16
125	2·96±0·09	6·665	6·679	16
500	3·55±0·08	7·081	7·090	16
2,000	4·25±0·06	7·518	7·505	16
8,000	5·03±0·09	7·952	7·910	16
32,000	5·73±0·10	8·307	8·321	16

All glucose uptakes with insulin were significantly greater than the basal glucose uptake. Each increase in dose recorded produced a significant increment in response.

The mean plasma insulin activity by the single standard method was 13.5 milliunits per ml. (limits of error 12 to 19.8 milliunits per ml.); by four-point assays the mean plasma insulin activity was 12.4 milliunits per ml. (limits of error 6 to 24 milliunits per ml.). The experimental details and individual results are recorded in Tables II and III and Fig. 2.

TABLE II.—*Insulin Activity of Plasma from Normal Human Subjects 2½ Hours After Oral Glucose, as Assayed by the Single Standard Method*

Normal Human Subjects (Fed)	Blood Sugar	Glucose Uptake in Presence of		Plasma Insulin mU./ml.	Limits of error P=0·05	N
		Plasma Diluted 1:4	Insulin 2 mU./ml.			
1	103	3·95±0·17	3·52±0·23	20	8 to 53	12
2	77	4·18±0·03	4·03±0·08	11	5 to 28	12
3	102	4·14±0·04	4·02±0·27	10	4 to 26	12
4	72	4·16±0·17	4·10±0·14	9	3 to 26	12
5	80	4·27±0·12	3·84±0·22	19	6 to 62	8
6	89	4·65±0·14	4·51±0·14	10	3 to 32	8
7	90	4·26±0·42	3·76±0·11	22	8 to 63	11
			Mean:	13·50	12 to 19·8	(75)

N is total number of hemidiaphragms used for determining the mean glucose uptake in the presence of plasma and of insulin.

TABLE III.—*Insulin Activity of Plasma from Normal Human Subjects 2½ Hours After Oral Glucose, as Assayed by Four-point Assays*

Assay No.	Glucose Uptake with Insulin		Glucose Uptake with Plasma		Plasma Insulin mU./ml	Fiducial Limits P=0·05
	Concentrations		Dilutions			
	0·5 mU./ml.	2 mU./ml.	1 : 16	1 : 4		
1	3·14±0·18	3·84±0·22	3·48±0·19	4·27±0·12	16·7	7 to 38
2	2·93±0·12	4·51±0·14	3·10±0·14	4·65±0·14	10	7 to 14
				Mean:	12·4	6 to 24

Four observations at each dose level.
All glucose uptakes significantly greater than the basal glucose uptake.

Recovery of Insulin Added to Plasma In Vitro

In Table IV are recorded the results of experiments in which the insulin activity of insulin–plasma mixtures prepared *in vitro* was assayed. In these experiments insulin

TABLE IV.—*Recovery of Insulin Added In Vitro to Buffer-plasma Mixtures Prepared in the Usual Way*

Basal Glucose Uptake	Glucose uptake due to plasma with insulin added *in vitro* to give a total estimated concentration of 8·25 mU./ml.	Glucose uptake due to Insulin. Concentration, 8 mU./ml.
2·54±0·18 (4)	5·02±0·27 (6)	5·08±0·27 (6)
2·30±0·05 (4)	4·33±0·21 (6)	4·08±0·10 (6)

Both estimates performed with a single sample of normal human plasma collected 2½ hours after oral administration of 50 g. of glucose. Insulin content, 13 mU./ml.
Figures in parentheses = number of hemidiaphragms.
For first assay, estimated insulin content of insulin-plasma mixture is 7·7 mU./ml. (limits of error, P=0·05, 2 to 30 mU./ml.).
For second assay, estimated insulin content of insulin-plasma mixture is 12·6 mU./ml. (limits of error P=0·05, 3 to 33 mU./ml.).
Recovery of added insulin not significantly different from 100% in either case.

was added, *in vitro*, to buffer-plasma mixtures prepared in the usual way, to bring the insulin content to a calculated value of approximately 8 milliunits per ml. The glucose uptake of the diaphragm in this mixture was then compared with the glucose uptake of the diaphragm in the presence of insulin at a concentration of 8 milliunits per ml. The recovery of insulin added to plasma *in vitro* and assayed in this way did not differ significantly from 100%.

Insulin Activity of Normal Human Plasma Assayed in the A.D.H. Rat

Previous workers have reported the insulin content of normal human plasma, collected after a glucose meal, to be 0.34 milliunit per ml. (Bornstein and Lawrence, 1951b), 1 milliunit per ml. (Groen and Willebrands, personal communication), and 0.1 to 0.6 milliunit per ml. (Vallance-Owen and Hurlock, 1954). The value obtained by the rat-diaphragm assay described in this paper is considerably greater than these reported values.

The discrepancy between whole-animal methods and the rat-diaphragm technique described in this paper is illustrated by the assay using A.D.H. rats (Table V). In this experiment the change in blood sugar of A.D.H. rats over a period of 20 minutes following the intravenous injection of normal human plasma was measured. It was observed that plasma, assayed by the rat-diaphragm method to contain 13 milliunits of insulin per ml., had no effect upon the blood sugar of A.D.H. rats. By contrast 2 milliunits of insulin produced a highly significant fall of blood sugar in the same A.D.H. rats under similar experimental conditions.

TABLE V.—*Effects of Intravenously Administered Saline, Normal Human Plasma, and Insulin Upon the Blood Sugar of Alloxan-diabetic Hypophysectomized Rats*

Nature of Injected Material	Mean Fall of Blood Sugar ± S.E. Mean	No. of A.D.H. Rats	t	P
1. Saline (1 ml.)	−4·6±4·1	8		
2. Normal human plasma* (1 ml.)	−13·8±8·8	5	—	—
3. 2 milliunits of insulin in 1 ml. of saline	−41·5±5·2	5	*t* for 1 v. 3 is 9·3 *t* for 2 v. 3 is 6·8	<0·001 <0·001

* 1 ml. of this plasma possessed activity equal to that of 13 mU. of insulin in the rat-diaphragm assay.

Insulin Activity of Cysteine-treated Plasma

Du Vigneaud *et al.* (1931) observed that cysteine treatment inactivated insulin. Other workers who have used the rat-diaphragm assay for insulin have reported that cysteine will abolish the insulin activity of human plasma or serum. This observation has been confirmed in experiments in which normal human plasma was incubated with cysteine (concentration 20 mg. per ml.) for 12 to 18 hours. The experiments were controlled by simultaneous incubation of the same plasma in the absence of cysteine. It was observed that incubation with cysteine consistently abolished the insulin activity of plasma, whereas plasma incubated without cysteine still possessed significant insulin activity. It was observed in additional experiments that the basal glucose uptake determined in buffer incubated with cysteine was similar to the basal glucose uptake in untreated buffer. The results of typical experiments are recorded in Table VI. Some samples of cysteine-treated plasma were found to inhibit the glucose utilization of rat diaphragm, but this effect was not consistently seen (Table VI).

TABLE VI.—*Insulin Activity of Human Plasma After Dialysis and After Treatment with Cysteine as Detected by the Rat-diaphragm Technique*

Addition to medium of:	Change in Glucose Utilization	N	t	P
Dialysed normal human plasma	1·07±0·19	6	3·5	<0·02>0·01
Buffer incubated with cysteine	0·05±0·09	6	—	—
Normal human plasma (1)				
Incubated with cysteine	−0·57±0·10	6	4·40	<0·01
Incubated without cysteine	1·00±0·12	6	5·50	<0·01
Normal human plasma (2)				
Incubated with cysteine	0·14±0·21	6	—	—
Incubated with cysteine and dialysed	−0·14±0·22	6	—	—

Glucose uptakes expressed as increments over the basal glucose uptake ± S.E. of mean.
N is $N_1 + N_2 - 2$ where N_1 and N_2 are the number of hemidiaphragms used for determining the basal glucose uptake and the glucose uptake in the presence of plasma or other added material.
† All samples of plasma were random samples.

Samples of cysteine-treated plasma which had been dialysed against buffer for 18 hours, to remove residual cysteine, were also without insulin activity (Table VI). By contrast, untreated human plasma does not lose its insulin activity when dialysed against buffer (Table VI).

Discussion

Assay of Insulin by the Isolated Rat Diaphragm

The rat-diaphragm technique for the assay of insulin has not previously been critically investigated by conventional statistical methods. The results of statistical appraisal of the rat-diaphragm technique, reported in this paper, suggest that it is not a very precise method for the assay of insulin, though the index of precision ($\lambda=0.36$) compares favourably with that of some methods at present used for the bioassay of other hormones—for example, the tibial band assay for growth hormone. It is difficult to compare the results of this investigation of the rat-diaphragm assay for insulin with those previously reported, since other workers have not supplied comparable statistical data. The variance encountered in the experiments reported in this paper is similar to that found by other workers who have studied the glucose uptake of the isolated rat diaphragm—for example, see Ottaway (1953).

The sensitivity of the isolated rat diaphragm to insulin was found in these experiments to vary considerably from time to time and the variation in sensitivity was not necessarily seasonal; in disagreement with previous reports (*Groen *et al.*, 1952; Vallance-Owen and Hurlock, 1954). The minimum effective concentration of insulin in these experiments was 10^{-4} unit per ml., though some workers have claimed that as little as 5×10^{-6} unit of insulin per ml. will increase the glucose utilization of the isolated rat diaphragm (Groen *et al.*, 1952).

Specificity of the Rat-diaphragm Assay for Insulin in Plasma

Many workers have previously reported that the plasma of normal animals will increase the glucose uptake of rat diaphragm when added to the fluid in which the isolated diaphragm is suspended. This effect has been variously attributed to non-specific effects of plasma protein (Park, 1952), or to insulin in the plasma (Tuerkischer and Wertheimer, 1948; Groen *et al.*, 1952; Vallance-Owen and Hurlock, 1954).

Park attributed the insulin activity of normal rat plasma in the rat-diaphragm assay to non-specific effects of plasma protein, since he found that crystalline bovine serum albumin and A.D.H. rat plasma would stimulate the glucose uptake of the isolated rat diaphragm. However, these experiments do not prove conclusively that the effects of normal plasma are not due to insulin, since crystalline bovine serum albumin and A.D.H. rat plasma may well contain insulin. In this connexion Gemmill (1940) reported that crystalline ovalbumin did not increase the glucose utilization of the isolated rat diaphragm.

Groen *et al.* concluded from their experiments that the insulin-like activity of plasma from normal human subjects and dogs in the rat-diaphragm assay was due to *insulin*, since the activity was not found in plasma obtained from severely diabetic patients and depancreatized dogs. The validity of this conclusion is, however, doubtful, since Park (1952) and Bornstein (1953) have reported that the plasma of alloxan-diabetic rats contains endocrine factors which inhibit the glucose utilization of the isolated rat diaphragm. The failure of Groen *et al.* to detect insulin-like activity

*Groen and Willebrands (personal communication) have more recently concluded that this variation in sensitivity is not seasonal.

in the plasma of severely diabetic patients and depancreatized dogs, by the rat-diaphragm technique, may be due to the presence of inhibitors in these plasma samples and not to their low insulin content. The fractionation and identification of the material in human plasma responsible for its insulin-like activity in the rat-diaphragm assay would appear to merit urgent attention.

Insulin Content of Normal Human Plasma*

The insulin activity of normal human plasma assayed by the rat-diaphragm technique reported in this paper was found to be 13 milliunits per ml. This is considerably greater than the value of 0.34 milliunit per ml. reported by Bornstein *et al.* (1951b), who used the A.D.H.A. rat assay for insulin. This discrepancy between animal methods and the rat-diaphragm technique described in this paper is illustrated by the A.D.H. rat assay (Table V). In this experiment normal human plasma, assayed by the rat-diaphragm method to contain 13 milliunits of insulin per ml., was found to have no hypoglycaemic effect when injected into A.D.H. rats, though 2 milliunits of insulin produced a highly significant fall of blood sugar when injected into the same animals under similar experimental conditions. This discrepancy could be due to insulin antagonists in human plasma which antagonize the hypoglycaemic action of insulin in animals but which do not antagonize the action of insulin upon the isolated rat diaphragm *in vitro*, or it could be due to non-specificity of the rat-diaphragm assay for insulin in plasma. Some evidence for the former belief is provided by the report of Weitze and Hagedorn (Hagedorn, 1952). These authors, utilizing the fall in blood sugar of alloxan-diabetic hypophysectomized adrenodemedullated rats to assay insulin, reported the insulin activity of normal human plasma after acid alcohol extraction to be ten times the value obtained by Bornstein *et al.* (1951b) for untreated plasma. The high value could result from a separation of insulin from insulin antagonists in the plasma by the extraction procedure which these authors used.

The reason for the discrepancy between the values obtained for the insulin activity of normal human plasma by various workers who have used the rat-diaphragm assay for plasma insulin is not clear. It may be due to differences in specificity between diaphragms obtained from different strains of rat, since some workers have reported wide differences in the sensitivity of the isolated rat diaphragm to insulin. The high values reported in this paper are not due to minor modifications of the technique (Randle, unpublished experiments). Since Ottaway (1953) has reported that small quantities of growth hormone *in vitro* will enhance the glucose utilization of rat diaphragm, the high values for the insulin activity of normal human plasma reported in this paper may result from the presence of growth hormone in the plasma. The insulin activity of acromegalic plasma assayed by the rat-diaphragm method is considerably greater than the insulin activity of normal human plasma, and it may be that this difference is also attributable to the presence of growth hormone in the plasma (Randle, 1954a). The nature of the material responsible for the insulin-like activity of human plasma in the rat-diaphragm assay is being further investigated.

Summary

The claim of Groen *et al.* that normal human plasma will increase the glucose utilization of the isolated rat diaphragm has been confirmed and the evidence for attributing this effect to insulin in the plasma critically re-examined.

The rat-diaphragm technique has been critically explored as a quantitative assay for small amounts of insulin and applied to the determination of the insulin *activity* of normal human plasma. By this technique the insulin *activity* of plasma collected from normal human subjects after a glucose meal was found to be approximately 13 milliunits per ml. This estimate of the insulin activity of normal human plasma is considerably greater than those previously reported by other workers. The possible reasons for this discrepancy are discussed in brief.

The importance of specificity in bioassays for plasma insulin is stressed.

*Bioassay methods for insulin in plasma almost certainly measure the resultant of the contra-actions of insulin and insulin antagonists present in the plasma. For this reason the term *insulin activity* has been used in this paper in referring to the biologically determined *insulin content* of plasma.

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Meat hygiene was the subject of a recent seminar in Copenhagen organized by W.H.O.'s regional office for Europe. The following figures are given for the consumption of meat (carcass weight) in a year per head of population in different countries. The figures relate to 1952–3 unless otherwise stated.

Country	In Kilograms	In Pounds
Austria	41	90
Belgium and Luxembourg	45	99
Canada (1951–2)	66	146
Denmark	57	126
Finland	32	71
France	60	132
Germany (Federal Republic)	39	86
Greece	13	29
Ireland (Republic)	53	117
Italy	16	35
Netherlands	32	71
Norway	33	73
Sweden	50	110
Switzerland (1951–2)	47	104
Turkey (1951–2)	16	35
United Kingdom	47	104
United States of America (1951–2)	76	168
Yugoslavia	18	40

Meat is easily contaminated, and is an important source of food poisoning. According to figures collected at the seminar, in the United States from 1945 to 1947 32% of the food-poisoning outbreaks were due to meat. In England and Wales in 1950, 68% of the outbreaks affecting more than one person in which the source was identified were due to contaminated meat.

CONGENITAL HEART DISEASE

REPORT ON AN UNUSUALLY HIGH INCIDENCE IN ONE FAMILY

BY

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Congenital heart disease in more than one member of a family, although relatively uncommon, has been reported in the literature on a number of occasions. Abbott (1927) found 11 pairs of brothers and sisters, and Brown (1939) reported six instances. Taussig (1947) has seen four families in which more than one member was affected, and in two of these the condition was transmitted through more than one generation.

The purpose of this paper is to report four cases occurring in one sibship. This is exceedingly rare, and, so far as we can ascertain from the literature, has been reported only once previously. That was by Walker and Ellis (1940–1), who described a father and four out of eight children with persistent ductus arteriosus.

The Family

1. The eldest child was a boy aged 11 years. Signs of persistent ductus were discovered at routine school medical inspection. There was a typical Gibson murmur with thrill, and confirmatory radiological signs. He is awaiting operation.

2. A girl aged 9 showed no cardiac abnormality.

3. A boy aged 8. Signs of persistent ductus were discovered at routine school medical inspection. His lesion was more severe than that of the eldest child. Surgical ligation of ductus was successfully carried out.

4. A girl died in 1946 at the age of 6 months, from what was believed to be pneumonia.

5. A boy aged 5 showed no cardiac abnormality.

6. A boy aged 4. He was the third member of the family with persistent ductus. His was the most severe lesion of the three, there being marked cardiac enlargement and gross engorgement of pulmonary vessels. A successful operation has been carried out.

7. A girl died in 1949, only 13 days old. She was found dead in bed, and the cause was not definitely ascertained.

8. A girl aged 2 years showed no evidence of cardiac abnormality.

9. A boy, a "blue baby," died at the age of 7 weeks. He was seen by one of us a few days before death, and a diagnosis of congenital heart disease was made on the basis of central cyanosis and a moderately loud systolic murmur audible all over the praecordium.

Both parents were examined and found to be normal. There was nothing significant in their past histories; maternal rubella had not occurred, and circumstances were such that adequate nutrition was available. Consanguinity was not admitted. Only a limited investigation of ascendants was possible owing to the fact that most of them resided outside Ireland. No significant abnormality was detected in those examined.

Comment.—In this family there were four definite cases of congenital heart disease, three of them having persistent ductus arteriosus and one cyanotic disease of undetermined type. In addition, two other siblings died in infancy from causes which were not definitely ascertained. In view of the family history it is possible that a congenital heart lesion may have been a factor in the cause of death. The finding of such an incidence prompted us to review the literature and to consider possible aetiological factors, with particular reference to modern views on the subject.

Aetiology of Congenital Heart Disease

Congenital heart disease and congenital defects in general are believed to be due to genetic or environmental factors.

Genetic transmission, although difficult to prove, has always been considered important. In recent years, however, it has been shown that environment can play a part. Gregg (1941), in a series of 78 cases of congenital cataract occurring after maternal rubella during the early months of pregnancy, found that congenital heart lesions were present in 44. Swan *et al.* (1943) collected details of 31 congenital defects following maternal rubella, 17 of which were cardiac. Of these, seven had patent ductus; the others were varied, but cyanotic cases were not mentioned.

While this is strong evidence in favour of an environmental factor, it does not necessarily mean that maternal rubella is a very important factor in the transmission of congenital heart disease in general. In fact, the available evidence is to the contrary. In Campbell's (1949) series of 300 cases a history of maternal rubella was present in only four instances. In our own experience with a smaller number of cases no instance of maternal rubella has been found. Other environmental factors such as maternal nutritional deficiency have been suggested by Hale (1935) and Warkany (1944). Animal experiments by these workers have shown that congenital defects could be produced in the offspring if the maternal diet was deficient in certain vitamins. Can similar deficiencies cause congenital heart disease in man?

The answer would be obtained if the incidence of congenital heart disease in nutritionally deficient mothers as compared with the normal were known. Needless to say, this would have to be a large-scale survey, carried out as early as possible during pregnancy. So far as we are aware, such a survey has not been done, so that in the present state of our knowledge there is no evidence that maternal nutritional deficiency can cause congenital heart disease in man.

Genetic Factors

The best evidence of a genetic factor would be a positive family history. This is not forthcoming, and may be due to the fact that few women with congenital heart disease marry and have children (Campbell, 1949). However, as Campbell points out, the incidence in collaterals is more common than would be expected by chance. That would certainly be true of the family reported above, in which a genetic factor seems most likely. The collection of further evidence on this matter should be possible in future, in view of the developments of modern surgery. This applies particularly to persistent ductus.

We were unable, in a review of the literature, to obtain figures of the incidence of persistent ductus in population groups, with particular reference to schools. As additional evidence in favour of a genetic transmission of this lesion, we feel that the figures obtained by one of us at school medical inspection in County Roscommon may be of interest.

County Roscommon has a population of 68,000; land acreage is 608,540. The largest urban population is 2,000, so that the population is rural, mainly engaged in farming. The primary school-going population is 10,500, and of these 9,250 were examined routinely at school medical inspection over a three-year period. Fifteen cases of persistent ductus were observed among those examined. Twelve of these were confirmed subsequently by operation, and two of the remaining three by cardiac catheterization. Thus the incidence of persistent ductus among schoolchildren in this county is 1 in 616, or 1.6 per 1,000 examined between the ages of 4 and 15. There was no history of maternal rubella in any of these cases, and, in fact, rubella appears to be

uncommon in rural areas. Consanguinity was not admitted in any case. However, the tendency of farming or village populations to marry locally may be of importance.

This apparently high incidence in a rural population, if confirmed by a larger survey, would be additional evidence of a recessive genetic factor in the transmission of persistent ductus, and perhaps of congenital heart disease in general.

Summary and Conclusions

Details of four siblings with congenital heart disease are presented.

They include three cases with persistent ductus and one with cyanotic heart disease.

The aetiology of congenital heart disease is discussed and evidence indicating the importance of a genetic factor is presented.

Addendum.—Since this paper was sent for publication the diagnosis of persistent ductus in the boy aged 11 has been confirmed at operation.

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PANCREATICO-DUODENECTOMY FOR RELAPSING PANCREATITIS

BY

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The following case is reported as an example of the excellent result which may be obtained in relapsing acute pancreatitis following a pancreatico-duodenectomy. Although such a result does not help to elucidate the problem of the aetiology of this disease, freedom from further attacks should follow that operation. However, it is not denied that excellent results, either temporary or permanent, may also sometimes be obtained by the use of splanchnicectomy, choledocho-duodenostomy, etc.

For a variety of reasons a number of surgical measures have been proposed for the treatment of relapsing pancreatitis. These include cholecystectomy and choledochostomy (Mowat, 1951); choledocho-duodenostomy (Burt, 1953); choledocho-jejunostomy with total diversion of the bile (Barclay, 1950); splanchnicectomy, unilateral (Mallet-Guy and de Beaujeu, 1950) or bilateral (Connolly and Richards, 1950); subtotal gastrectomy, to cut off the secretin mechanism (Richman and Colp, 1950); sphincterotomy (Doubilet and Mulholland, 1948); and pancreatico-duodenectomy (Cattell and Warren, 1952). There is no doubt that pancreatico-duodenectomy would be the accepted method of treatment in cases with demoralizing pain if it were not for the magnitude of the operation and the risks it entails. Nevertheless, whatever operation is performed it should allow the pancreas and other abdominal viscera to be explored. It is especially important to determine whether or not the gall-bladder and common bile duct are normal.

According to Horton (1950) the first successful pancreatico-duodenectomy for pancreatitis was carried out in 1944 by Clagett. Horton was of the opinion that pancreatitis should be treated by pancreatico-duodenectomy only in most exceptional cases. On the other hand, in 1952 Cattell and Warren concluded that of the procedures they had used pancreatico-duodenectomy had given the best results, and they considered it the current method of choice in the treatment of relapsing pancreatitis.

Case Report

A man aged 40 was referred to me by Dr. R. Jennaway and was admitted to Sydney Hospital on May 23, 1953. For 18 months he had complained of attacks of epigastric pain, often extremely severe and sometimes lasting for 24 hours, but not related to meals. The pain extended to both sides of the abdomen and was only partly relieved by morphine. Rarely, it radiated to the back. At first the attacks occurred every two to three weeks, but for the previous three months attacks occurred every two or three days. On a few occasions vomiting accompanied the pain. Between the attacks his appetite had been good. He had never been jaundiced, and Graham's test showed no abnormality in March, 1952. On February 10, 1953, laparotomy revealed an enlarged indurated head of the pancreas, and the surgeon considered this to be malignant. Other viscera, including the biliary tract, appeared normal, and there was no evidence of any metastasis. Three days later during a severe attack of pain the urinary diastase level was 100 units. Despite the severity of the attacks of pain there was no evidence of alcoholism or drug addiction.

On May 23 his general condition was still good despite the loss of 2 stone (12.7 kg.) in weight during the previous three months, and examination of the abdomen showed no abnormality. His serum bilirubin level was 0.1 mg. per 100 ml. On May 26 a barium-meal examination showed that the stomach was empty in four hours. A deformity with some constriction of the second part of the duodenum was present, and this was producing a mild partial obstruction. (Similar appearances have been reported by Cattell and Warren (1952) in relapsing pancreatitis.)

On May 28 a pancreatico-duodenectomy was performed. Through an upper midline incision the pancreas was palpated and the replacement of its head and body by a hard irregular mass was confirmed, but the consistency of this mass was not uniform. The terminal portion of the tail of the pancreas appeared normal. The mucosa of the duodenum was intact though slightly hypertrophic, and no obstruction of the lumen of the duodenum was demonstrable. The biliary tract and liver appeared normal. There were a few small soft lymph nodes along the upper border of the pancreas, but no definite metastasis was detected.

The peritoneum to the right of the second part of the duodenum was incised, the stomach was divided immediately proximal to the pylorus, and the supraduodenal portion of the common bile duct was divided. The duodenum, together with the head and the body of the pancreas, was dissected free from the superior mesenteric vessels and other structures, and the tail of the pancreas was divided through what appeared to be normal pancreatic tissue about an inch (2.5 cm.) to the right of the hilum of the spleen. Reconstruction was then carried out in the order shown in the diagram. The end of the jejunum was closed about a small tube and was sutured to the peritoneum at the upper end of the abdominal wound. The inner end of this tube (which contained several holes) was passed down the jejunum and into the common bile duct, while its outer end was brought out through the wound. The anastomosis between the common bile duct and the jejunum was made with an outer interrupted layer of cotton sutures and an inner continuous layer of 00 catgut. The cut end of the remnant of the pancreas was fixed into an incision in the side of the jejunum with two layers of interrupted cotton sutures. No

tube was inserted into the pancreatic duct, which did not appear to be dilated. The severed end of the stomach was anastomosed end to side to the jejunum with an outer interrupted layer of cotton sutures and two continuous inner layers of 00 catgut. A drainage tube was inserted down to the area from which the head of the pancreas had been removed.

The pathologist (Dr. L. R. Finlay-Jones) reported that the excised specimen consisted of a segment of duodenum

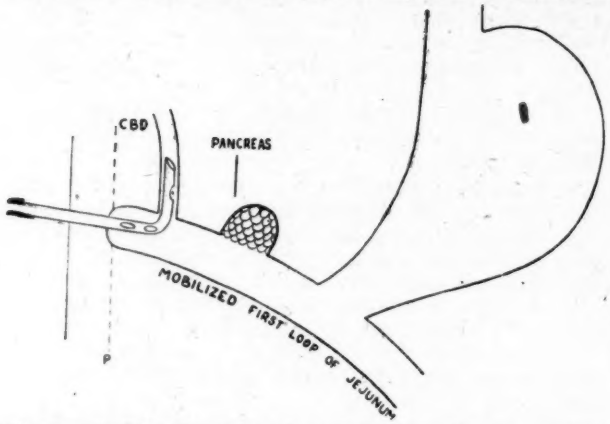

Diagram showing the order of reconstruction after pancreatico-duodenectomy. The remnant of the pancreas was implanted end to side in the jejunum between the common bile duct (CBD) and the stomach. The end of the jejunum was closed around a tube and then fixed to the parietal peritoneum (P).

15 cm. long and 3 cm. in diameter, attached to which was a hard irregular piece of pancreas 8.5 cm. long and 5 cm. in diameter, and containing a cyst about 1.5 cm. in diameter. The ampulla of Vater and the main pancreatic duct were patent. Microscopical examination showed that the pancreatic parenchyma was traversed by bands of cellular scar tissue and granulation tissue. There were collections of inflammatory infiltrate consisting of eosinophils, plasma cells, and polymorphs; and pigment-containing histiocytes were conspicuous in many regions. The muscle coat of the attached duodenum showed similar inflammatory changes. The appearances were consistent with recent attacks of pancreatitis. No evidence of carcinoma was found.

For the first 48 hours after operation the stomach was aspirated, and at the same time 4% glucose in N/5 saline was given intravenously. Thereafter the diet was increased gradually. Only a few ounces of bile a day drained from the tube in the common bile duct. This tube was removed after eight days, and the wound was healed within a further five days.

On June 19 the serum bilirubin level was 0.5 mg. per 100 ml. and a glucose-tolerance test gave readings of 98, 105, 128, 117, and 120 mg. per 100 ml.; there was no glycosuria. On June 24 the dried faeces contained total fat 57% (unsplit fat 42%, split fat 15%); and the urinary diastase level was 5 units.

Convalescence was uneventful. The patient was discharged home on June 27 with the wound healed, and has remained symptom-free. He resumed work as a mechanic on July 13.

Discussion

Prior to operation the lack of jaundice, the recurrent attacks of severe abdominal pain, the well-being of the patient, and the elevated urinary diastase during an attack of pain all suggested a diagnosis of relapsing acute pancreatitis rather than carcinoma of the pancreas. At operation the small areas of calcification, which incidentally had not been shown by radiography, the lack of uniform hardness of the gland, and the absence of metastases were also in keeping with the former diagnosis.

Pain is a frequent accompaniment of carcinoma of the pancreas, but it is not usually in the form of intermittent severe attacks. Also, the urinary diastase level is rarely more than slightly raised in the presence of a carcinoma of the pancreas. In this case the destruction of the pancreas had not been extreme and had not led to diabetes or to steatorrhoea. Even after operation no insulin or pancreatin had been required.

Biopsy of the mass in the pancreas was not performed, and is probably never indicated. There is always the doubt whether the portions selected for examination are representative; and biopsy may be followed by dissemination of malignant cells or a pancreatic fistula may develop.

Although the mucosa of the pyloric antrum was retained, its resection may be advisable, as the chance of jejunal ulceration would then be reduced. However, this patient has had the good fortune not to develop that or any other complication.

Because of the high operative mortality rate and the high recurrence rate doubt has been thrown on the possibility of cure of carcinoma of the pancreas by pancreatectomy (Cattell and Pyrtek, 1949). It is, however, reasonable to assume that the mortality rate for pancreatico-duodenectomy will be much less in relapsing pancreatitis than in patients with carcinoma of the pancreas, and it may be concluded that pancreatico-duodenectomy has a place in the treatment of relapsing pancreatitis whenever there is any doubt about the coexistence of a carcinoma or when the condition has failed to respond satisfactorily to other methods of treatment.

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PANCREATICO-DUODENECTOMY

OPERATION ON TWO ELDERLY PATIENTS

BY

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The two patients with carcinoma of the head of the pancreas detailed below may be regarded as rather elderly to undergo pancreatico-duodenectomy. They were aged 67 and 70 years, and their rapid recovery demonstrates that age alone is no bar to the performance of this operation in patients otherwise suitable. The second case has the additional interest that a subtotal gastric resection for haematemesis had been carried out six months earlier.

Case 1

A woman aged 67, with a four-weeks history of jaundice varying in intensity, had a dull pain deep in the right hypochondrium but no colic; no vomiting; anorexia. She enjoyed fatty food and had had no dyspepsia prior to the onset of jaundice. She had noticed that the stools were pale and the urine was dark in colour. There was no loss of weight. Appendicectomy had been performed in 1917.

On examination a moderately obese woman, deeply jaundiced but otherwise apparently well, was seen. Her blood pressure was 196/90, Hb 95%. Her heart was slightly enlarged; the respiratory system was normal. The abdomen was well covered; there was no tenderness or guarding. The liver was just palpable below the costal margin; the gall-bladder was tense and distended. A diagnosis of carcinoma of the head of the pancreas was made.

Operation.—On May 5, 1952, under general anaesthesia, the abdomen was explored through a right paramedian

incision. The liver was normal but the gall-bladder and bile ducts were distended. There was a hard inelastic nodule in the head of the pancreas. Nothing else abnormal was found. Mobilization of the duodenum and the head of the pancreas revealed that the growth was much larger than had at first been suspected. Further mobilization showed that the tumour was operable, and pancreatico-duodenectomy was performed. Reconstruction was effected by bringing up a loop of proximal jejunum through the transverse mesocolon and anastomosing the apex of the loop to the common bile duct, end to side. The divided body of the pancreas was implanted into the side of the jejunum distal to the choledocho-jejunostomy and, distal to this again, intestinal continuity was restored by fashioning a gastro-jejunostomy. The abdomen was closed with drainage. The post-operative course was uneventful, neither a biliary nor a pancreatic fistula developing.

Pathological Report.—"The specimen shows a tumour in the head of the pancreas surrounding a major pancreatic duct and incompletely obstructing it. The common bile duct also shows some compression, but the mucosa is intact. A few adjacent lymph nodes contain deposits of tumour. Histological examination shows an adenocarcinoma of pancreas of mucus secretory type."

This patient lived an active and comfortable life for ten months.

Case 2

A woman aged 70 had undergone an emergency partial gastrectomy for haematemesis six months earlier; a retrocolic anastomosis, afferent loop of jejunum to lesser curve of stomach and incorporating a Hofmeister valve, was used. She made a good recovery and was discharged from hospital apparently fit and well. Two months after gastric resection the stools became loose, pale, offensive, and frequent. Three months later she became jaundiced; at the time of admission this was less deep. The urine was dark in colour. She lost weight. Her appetite was good and she had no aversion to fatty foods.

On examination, a thin woman, deeply jaundiced, was seen. The epigastric scar was soundly healed, the liver was not enlarged; the gall-bladder was not palpable. The stools were negative for occult blood; the Van den Bergh reaction was direct positive; serum bilirubin, 10 mg. per 100 ml.; alkaline phosphatase, 31 units; colloidal gold +. The jaundice got progressively deeper and the liver and gall-bladder became palpable. A diagnosis of carcinoma of the head of the pancreas was made.

Operation.—On May 5, 1953, under general anaesthesia, a right paramedian incision was made. The gall-bladder and bile ducts were distended and contained clean concentrated bile. The common bile duct was not involved in any reaction secondary to the manipulations of the partial gastrectomy; the duodenal stump was free and mobile. An indurated tumour in the head of the pancreas was thought to be a carcinoma and was found to be operable. The body of the pancreas was fibrosed and scarred where it had been involved by the gastric ulcer. Pancreatico-duodenectomy was performed; the site of section of the pancreas coincided with the scarred area.

Reconstruction.—Intestinal continuity existed as a result of the gastrectomy. The short proximal loop of jejunum was anastomosed end to end with the common bile duct; as this left little room above the gastro-jejunostomy for implantation of the pancreas, that structure was oversewn and was not reimplanted. The peritoneal cavity was drained.

Pathological Report.—"The specimen shows a cellular tumour in the pancreas, microscopically a carcinoma. In some areas this shows acinar pattern and in others a pattern of duct carcinoma."

The patient made a rapid recovery. A biliary fistula did not develop, but from the fourth day there was a discharge of pancreatic ferments which was profuse for ten days and then rapidly dried up. The patient left hospital four weeks after operation; her condition at the time of writing is discussed below.

In this case carcinoma of the pancreas was almost certainly present at the time of gastric resection. However, as this was an emergency operation undertaken to control haemorrhage, further exploration was not performed when the cause of bleeding, a large active gastric ulcer, had been found.

Discussion

The classical description of jaundice due to carcinoma of the head of the pancreas as progressive and painless is no longer accepted as invariable; each of the cases reported here showed variation. It is true, however, that marked fluctuation in depth of jaundice is more common with ampullary growths than with carcinoma of the head of the pancreas proper.

It is apparent that with fit patients age need not necessarily be a contraindication to operation. These patients, aged 67 and 70, were both remarkably well after operation. The first patient was not given more than sips of water by mouth for several days, and it is possible that her early post-operative course was conducted with excessive caution. For the second patient, on the other hand, it was possible to discontinue intravenous fluids after 24 hours, there being a satisfactory gastro-jejunostomy as a result of her previous operation. In this case it was pleasing to find that the partial gastrectomy did not increase the difficulty of the pancreatico-duodenectomy; rather it simplified matters, as the mobilization was partly done and intestinal continuity already existed. The healed well-functioning anastomosis proved of great value, enabling the patient to take nourishment by mouth, without risk, at an early stage in the post-operative period, and excluded the necessity for the prolonged use of the potentially lethal form of therapy euphemistically termed intravenous alimentation.

So useful was the antecedent gastro-jejunostomy found to be that I would be inclined to follow Whipple, Parsons, and Mullins (1935) in employing it as part of the first stage in those cases considered to require a staged operation. All that is necessary is transection of the stomach followed by gastro-jejunostomy, employing an afferent loop of jejunum long enough to take, at the second operation, the pancreas and common bile duct. Apart from closure of its severed end, the distal segment of stomach need suffer no interference, thus leaving the operative field undisturbed for the second stage. However, a one-stage operation, where possible, is infinitely preferable.

Many forms of reconstruction have been described, and from them three principles have emerged: (1) the gastro-jejunostomy should be distal to the entrance of the common bile duct and the pancreas; (2) the common bile duct, not the gall-bladder, should be anastomosed to the jejunum; and (3) the pancreatic stump should be reimplanted. The third principle was not followed in Case 2, as, in the peculiar circumstances, there was little bowel readily available for reimplantation of both common bile duct and pancreas; also the body of the pancreas was so scarred at the site of section that its duct could not be identified. In this case the pancreatic fistula persisted for only two weeks, and it seems possible that the fortunately short period may be accounted for by the fact that the pancreas was already fibrosed at the site of transection.

Whitfield, Gourevitch, and Thomas (1952) investigated the metabolic effects of total pancreatectomy. They obtained 83% fat absorption when giving 11.5 g. of pancreatin a day, and thus demonstrated that, while reimplantation of the pancreas may be highly desirable, satisfactory fat digestion can be obtained by extraneous means. Brunschwig (1952) does not practise pancreatic reimplantation, and claims satisfactory function even without replacement therapy. Unfortunately my second case does not support this claim, as the patient continues to have frequent stools and has not regained weight. It is probable that the combination of pancreatico-duodenectomy—without pancreatic reimplantation—and partial gastrectomy puts too great a strain on the

remaining digestive function: it seems that the rapid passage of food through the small bowel due to the gastric resection does not allow enough time for the impaired digestion to achieve maximum results. Consequently, despite the fact that this patient has a very large appetite and takes a pancreatin compound by mouth, she hovers close to the verge of starvation. Her condition is worthy of note, as there has been some demand for extensive gastric resection to be incorporated with pancreatico-duodenectomy in an attempt to eliminate the stomal ulcers which sometimes occur. This case indicates that such a course would not be without its own hazards.

Brintnall (1952) reported a series of cases in which he used a form of reconstruction essentially that described by Child (1944); this entails telescoping the pancreatic stump into the open end of the jejunum; below this the common bile duct is implanted end to side, and lower still the gastro-jejunostomy is formed. No fistulae developed and the method appears to be very satisfactory. Brintnall also advocates mobilization of the portion of the pancreas to be removed from left to right; this, he maintains, gives the greatest possible exposure of the portal vein.

Is there a place for pancreatico-duodenectomy in the surgeon's repertory? There has recently been some suggestion that so extensive an operation is not worth while for carcinoma of the head of the pancreas, because the post-operative survival is generally short. This is a fallacious argument; palliation is at times the sole aim of surgery, and, though not so in this instance, it should be noted that effective palliation is obtained even when life is not greatly prolonged. Two patients have been observed following short-circuit operations; they became, within four months, impressively miserable from the pain of their growths. Suffering can be avoided by resection, and this operation should be done for all operable cases. Furthermore, Orr (1952) reports an average survival of 15 months with the radical operation, in contrast to 4.4 months following palliative procedures.

We must always seek to progress, and there is no doubt that dissatisfaction with results obtained is a greater stimulus to further endeavour than is the counsel of despair which labels a condition beyond the scope of surgery and incurable. Neither should it be overlooked that, in regard to carcinoma of the pancreas, Brunschwig, one of the pioneers in this field and an advocate of radical excision, reported a seven-year survival for carcinoma of the head of the pancreas proper.

Dodd wrote in 1949, "I make a plea that in cases in which painless jaundice has been present for a month the possibility of carcinoma of the pancreas should be considered and a surgical opinion sought." This statement merits repeating because it indicates the correct line to be followed if cases are to come to surgery early enough to allow a determined attack to be made on the growth with hope of success.

Summary

Two successful cases of pancreatico-duodenectomy for carcinoma of the head of the pancreas, in patients over 65 years, are reported. One patient had recently undergone emergency gastric resection for haemorrhage.

The place of the operation in present-day surgery is discussed; it may require to be made more radical.

The importance of early laparotomy for patients with undiagnosed or painless jaundice is stressed.

I am grateful to Dr. J. McMurray for the pathological reports.

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Medical Memoranda

A Case of Complete Aortic Atresia with a Dissecting Aneurysm

Coarctation of the aorta is a reasonably common form of congenital cardiac abnormality. Abbott (1928) found 142 in her classic series of 1,000 cases. Wood's (1950) series of 200 cases contained 16 coarctations of the aorta. Until recently the diagnosis was of academic interest only; now that surgery may in certain cases effect a cure it is important that the diagnosis should be made as soon as possible. The following case is of sufficient interest to merit publication.

CASE REPORT

The patient was a man aged 33. As a child it was noticed that his heart was abnormal. Unfortunately no details are available. He remained well and joined the regular Army, in which he served for 12 years, passing a special medical examination in the Royal Engineers as fit for diving operations. He had no symptoms until the last month of his life, when he noticed that he became very tired on exertion; two days before death he developed flatulence. On the day of his death he was cycling home from work when he was seized with a violent precordial pain which went through to his back. He managed to dismount and was brought to hospital in a passing car.

Photograph of the specimen.

On admission he was cold, shocked, and still in great pain. His pulse was regular with a rate of 120, and his blood pressure was 70/50. A well-marked presystolic triple rhythm was heard at the cardiac apex; there were no murmurs. An E.C.G. showed nodal rhythm with bundle-branch block and raised ST segments in Lead I and the precordial leads. The tracing was a poor one owing to the patient's restlessness. His general condition precluded further examination.

He was given morphine, and in view of the profound shock a plasma infusion was started, but was stopped owing to a rigor after half a pint (285 ml.) had been given. He died a few hours later, the clinical diagnosis resting between a dissecting aneurysm and a cardiac infarct.

Post-mortem examination showed gross left ventricular hypertrophy. The aortic valve was bicuspid. There was complete aortic atresia at the usual site of the adult type of coarctation of the aorta. The intima showed a split just above the aortic valve, and the dissecting aneurysm had burst through the aorta, producing a large haematoma round the base of the great vessels (see Fig.). This could well have pressed on and obstructed the left coronary artery, but no myocardial infarct was seen. The collateral circulation was not dissected.

COMMENT

Coarctation of the aorta is of two types. The infantile type consists of narrowing of the whole isthmus of the aorta from the left subclavian artery to the ductus arteriosus; the

circulation depends on a patent ductus arteriosus, and is compatible only with a few weeks or months of life. The adult type consists of a localized narrowing about the level of the ductus arteriosus, and these patients may live for many years; in Abbott's series the ages of death varied from 3 to 92 years, with an average of 32. In 200 cases which came to necropsy the atresia was complete in 47, extreme (under 6 mm.) in 108, and moderate in 45. The figures of Reifenstein *et al.* (1947) are similar, the average age at death being 35. Both workers found that rupture of the aorta was a common cause of death, especially among younger patients. Abbott found it 40 times in her 200 cases examined at necropsy, and all Reifenstein's cases occurred between the ages of 10 and 30. The rupture generally occurred in the ascending aorta, but was sometimes seen at, or near the site of, the obliterated ductus. Here the aorta was often dilated at the emergence of the intercostal arteries, or kinked by the ligamentum arteriosum. Histological examination of the aorta nearly always showed medial degeneration. There was interruption and diminution of the elastica and muscle, with fatty and hyaline degeneration. The connective tissue was increased: Gore and Seiwert (1952) found this in 85 cases of dissecting aneurysm, not necessarily associated with coarctation; hypertension was present in only 58% of cases.

The recognition of coarctation of the aorta is not difficult if the diagnosis is kept in mind. Hypertension is present in most cases, but may be only slight in children. A systolic murmur is often heard over the front and back of the chest, where the enlarged collateral circulation may be seen and felt; the unusual site of the murmur is most suggestive of a coarctation. The femoral pulses are absent, or are feeble and delayed. Radiology may show notching of the lower borders of the ribs due to the hypertrophied intercostal arteries.

Surgical treatment of the condition is generally undertaken in children and young adults; therefore it is necessary to make the diagnosis early, generally before any symptoms arise.

If the femoral arteries are palpated as a routine during a medical examination cases of coarctation of the aorta will not be missed.

I wish to thank Dr. E. S. Duthie for the pathological examination and Mr. R. P. Welch for the photograph of the specimen.

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Rupture of a Congenital Solitary Kidney

The disaster of severe trauma to a solitary kidney of congenital origin is fortunately rare. Orkin (1950) has collected seven examples. The following case is a reminder of this tragic possibility.

CASE REPORT

A man aged 63, returning from his work in a dockyard, tripped and fell across a heavy chain, injuring his left side. He walked home and, fearing he had injured his ribs, then walked to hospital. The casualty officer found severe tenderness over the left loin and left lower ribs, and took the wise precaution of inspecting his urine. Gross haematuria was found and the patient was admitted. Shortly after admission the pulse rose and the blood pressure fell. In half an hour an enormous tumour grew in the left loin and projected anteriorly, to be clearly delineated like a huge hydronephrosis. Blood transfusion failed to control the falling blood pressure, and there was every justification for a rapid transfer to the operating theatre.

Operation.—Through a left lumbar incision a huge perirenal haematoma was explored. In the midst of free fluid, blood, and clot lay a lacerated kidney with its pedicle almost completely detached. The kidney was lifted out and the bleeding pedicle readily controlled. The cavity formed by the haematoma extended more than an inch (2.5 cm.) beyond the right margin of the vertebral column. Palpation to the right was thought to confirm the presence of a right kidney. With control of haemorrhage the general condition improved rapidly. In all, six pints (3.4 litres) of blood was given.

Post-operative Course.—As no urine was voided twenty-four hours after operation a catheter was passed and 1 oz. (28 ml.) of bloody urine withdrawn. The blood pressure was normal, and with no further secretion by the end of the second day it was noticed that the right testicle was not palpable in the scrotum or elsewhere. On the fourth day cystoscopy was performed and in a contracted bladder no right ureteric orifice could be found. The absence of a right kidney was now presumed. The patient died on the tenth post-operative day. A post-mortem examination confirmed the complete absence of the right kidney and ureter. The right adrenal gland was present. The bladder was small and thick-walled, with poor development of the right side of the trigone. There was a small but complete right intra-abdominal testicle. Examination of the left kidney confirmed that it was split transversely through the hilum and that the vascular pedicle was almost completely torn.

COMMENT

In this case the rapid deterioration from haemorrhage necessitated urgent operation. It was not justifiable to attempt intravenous pyelography, although it is agreed that this practice has an established place in the management of renal injury. Orkin (1950), amongst many others, has stressed how this investigation may determine the necessity or otherwise for immediate exploration of the damaged kidney, and how valuable it is in revealing a functioning kidney on the other side. It would have been possible to do a cystoscopy before nephrectomy in the above case, and had the absent testicle been noted suspicion of a solitary kidney might have been aroused. The fact that the injured kidney could not be saved does not forgive this inadequate pre-operative management. In other circumstances recognition of a solitary kidney might have encouraged an attempt at suture or even vascular repair.

Hamilton and Peyton (1950) reported a case in which by pyelography and cystoscopy it was recognized that an injured hydronephrotic kidney was solitary. Bleeding persisted and the kidney had to be explored: a 10-cm. laceration was sutured and the kidney saved. Orkin (1950) described the radiological and cystoscopic confirmation that an injured kidney was solitary. In this case operation was not required and conservative treatment was successful.

Congenital solitary kidney is not unduly rare. Collins (1932) collected 581 examples, and Longo and Thompson (1952) suggested that the necropsy rate is about 1 in 1,000 cases and the clinical incidence about 1 in 1,500 cases. If we add the possibilities of hypoplastic or maldeveloped kidneys, of kidneys destroyed by disease, and of kidneys removed by previous nephrectomy, injury to a solitary kidney is an accident worth consideration. The solitary kidney may be damaged rather more readily, as it is usually larger and therefore less protected than a normal kidney. Longo and Thompson (1952) have shown a high incidence of disease in the congenitally solitary kidney. This, too, may make it prone to injury—hydronephrosis being a common complication. Anomalies of the genital tract are common in females with solitary kidney; in males the association occurs in only 10% of cases. This is the second case I have seen in which an absent testicle was noted with a congenitally absent kidney.

JOHN A. SHEPHERD, M.D., Ch.M., F.R.C.S.Ed.

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Reviews

IN HONOUR OF CHARLES SINGER

Science, Medicine, and History: Essays on the Evolution of Scientific Thought and Medical Practice. Written in honour of Charles Singer. Collected and edited by E. Ashworth Underwood. Volumes I and II. (Vol. I: Pp. 563, illustrated. Vol. II: Pp. 646, illustrated. £11 11s. the set.) London: Geoffrey Cumberlege (for Oxford University Press). 1953.

The occasion of the presentation of these two volumes of *Essays* to Dr. Charles Singer has already been described in this *Journal*. To do justice to this splendid tribute to a great medical historian is no easy task. A brief biography of Dr. Singer with a bird's-eye view of his achievements, an introduction by Sir Arthur MacNalty, ninety learned essays, and finally a list of Dr. Singer's 412 contributions to the literature of medicine and medical history—all this can scarcely be treated adequately within the compass of an ordinary review.

Dr. Ashworth Underwood must have conceived the idea of these volumes and have started collecting the essays a good many years ago. Fourteen of his contributors have died without seeing the completed book, and the difficulties which oppress the editor of any composite volume are notorious. Dr. Underwood is therefore to be congratulated on bringing his heavily laden ship to harbour and to be thanked for the treasures it contains.

The essays in these two large volumes are as various in subject as the interests of Dr. Singer himself. They are divided into eight books, the first seven covering chronological periods, the eighth dealing with matters that could not be thus accommodated. The first book treats of the Ancient World, beginning with an illuminating essay by Professor Gordon Childe on "The Constitution of Archeology as a Science." Mr. Warren Dawson provides an authoritative account of "Egypt's Place in Medical History," in which he makes clear what were the original sources of medical and anatomical knowledge and how it was inextricably mixed with magic. The practice of mummification allowed the study of comparative as well as human anatomy and pathology, and so fostered the true beginnings of medical science in the Valley of the Nile. Another paper by Dr. Chauncey D. Leake and others reveals the fascinating contents of the Hearst Papyrus, from which it is clear that treatment of fractures by plaster casts was well established by 1500 B.C. An essay by the late Professor George Gask and the Rev. John Todd traces "The Origin of Hospitals," and from this it appears that no hospital in the true sense existed before Christian times and that probably they did not begin until the first half of the fourth century A.D. Dr. Wilfred Bonser's contribution on "General Medical Practice in Anglo-Saxon England" is remarkably interesting for its demonstration of how the curing of disease was virtually a monopoly of the Church. Saints and their relics were systematically exploited as the supernatural means of exorcising what was assumed to be a supernatural visitation. Christ had shown the way by His miracles, and the holiness of His saints was manifested by their power to do the same. Ignorance of the nature of disease was common to ecclesiastical and lay practitioners and their understanding of the remedies they used was correspondingly primitive. Bloodletting had been handed down from classical times, and, being connected with the doctrine of humours, was used indiscriminately and survived in medicine for more than another millennium. Dr. Henry Sigerist writes a characteristically interesting and important paper on the contents of the remarkable manuscript at Johns Hopkins University containing a gynaecological collection made by Johannes Hartlieb, a Bavarian court physician, in the middle of the sixteenth century. Dr. Castiglioni wrote not long before his death on Pliny's great book and the School of Ferrara, studying particularly the work and influence of Leonicenus. Mrs. Arber contributes a learned and interesting paper on mediaeval herbalism and its progress to modern botany. Among the non-medical essays Professor F. J. Cole's history of Dürer's rhinoceros is particularly attractive. The animal passed through many pictorial transformations and in 1617 appeared as the crest of the Society of Apothecaries, its horn being then still of importance in the pharmacopoeia. Three papers on Vesalius—"Some Vesalius Studies" by Dr. Monteiro, of Oporto, "Vesalius and the Galenists" by Dr. Ashley Montagu, and "Vesalius: Imperial Physician" by Drs. O'Malley and Saunders—keep alive the subject of the great anatomist. Fernel's name is commemorated in Dr. Long's study of his ideas on tuberculosis. Dr. Galdston, of the New York Academy of Medicine, extracts much of interest regarding psychiatry in his survey of the writings of Paracelsus, who clearly used psychotherapy very much in the modern manner. Sir Arthur MacNalty pays his tribute to "Sir Thomas More as Student of Medicine and Public Health Reformer." Dr. Walter Pagel covers a wide field in seventeenth-century biological thought by consideration of the reaction of seven important writers to Aristotle. These include Glanvill, Charleton, Harvey, and Glisson. The importance of Glisson as a thinker in addition to his anatomical pre-eminence is well brought out.

The second volume covering the later seventeenth century, the eighteenth and nineteenth centuries, and the *Conspectus Generales* is perhaps less exciting than the first, but there is still plenty to attract the eye of a medical reader. Dr. Ashworth Underwood chooses for his own contribution an account of Gottfried von Berger and his textbook of physiology published in 1701. Mr. Johnston Abraham writes an all too short account of John Fothergill. Professor Cave draws attention to the fact that it was really Sir Richard Owen who first described the parathyroid glands, having dissected them in a rhinoceros in 1849. The credit is usually given to Sandström's monograph of 1880. Dr. Dorothy Turner examines the work of that extraordinary man, Sir Thomas Young, on the eye and vision. His dictum that "the longer a person lives the less he gains by reading" should not be a deterrent to the perusal of the volumes under review. The names of Professor K. J. Franklin, Dr. Major Greenwood, Dr. Douglas Guthrie, Professor J. F. Fulton, and Sir Charles Scott Sherrington among the writers of *Conspectus Generales* is sufficient evidence of their value.

Attention has here been directed chiefly to the contributions of medical interest, but this does not imply that those covering allied sciences are of any lesser significance. This splendid work is profusely illustrated, and, though the price seems high, the buyer may be assured that he is getting his money's worth. The full indexes provide an essential guide to the whole.

GEOFFREY KEYNES.

ANTIBIOTIC THERAPY

Recent Advances in Chemotherapy. Vol. III—Antibiotics. By F. C. O. Valentine, F.R.C.P. and R. A. Shooter, M.A., M.D. (Pp. 292, illustrated. 27s. 6d.) London: J. & A. Churchill. 1954.

The late Dr. G. M. Findlay had planned that the third edition of *Recent Advances in Chemotherapy* should be in four volumes, of which two had appeared before his death. The present authors have shouldered the main outstanding task, and the series now covers most of its immense subject, the chief hiatus being the absence of any section devoted to the sulphonamides.

Antibiotics do not belong exclusively to any one branch of medical science; clinicians, microbiologists, and pharmacologists are all entitled to write about them and have done so. Which of them can write the most useful book is a matter of opinion. The microbiologist starts with some advantages. Antibiotics are, after all, microbic products, and it is his business to understand them. Moreover, bacteria are his daily companions, and their behaviour in the presence of antibiotics is variously and vividly illustrated in cultures the examination of which now occupies much of his time. If at the same time he is in close touch with, and sometimes advising, numerous clinical colleagues,

perhaps in hospitals where new antibiotics are receiving their first trials in this country, his knowledge of the more difficult aspects even of clinical application may exceed that of the individual clinician.

This book is the product of such experience, and is the first satisfying one of its size on this subject to appear—at least to a reviewer who views these matters from the same standpoint. It is quite remarkably up-to-date: there is a reference to a paper which appeared in November, 1953—four months before publication. It deals thoroughly and soundly with all the specific infections in which antibiotic treatment is indicated and, regionally, with venereal diseases, infections of the lung, meninges, bowel, and urinary tract, but not with wound infections as such, or those of the eye, nose and sinuses, skin, or uterus. It is in these directions that expansion in further editions might enhance the value of the book, although it may well be argued that, since chemotherapy should be directed against the micro-organism rather than the particular type of disease, a regional approach is superfluous unless special techniques are involved. The index needs expansion, and more needs now to be said about reactions to penicillin: so-called anaphylactic shock, which has been fatal in many recently recorded cases, is not mentioned.

The table of sensitivities of 22 species to eight antibiotics and the chapter on the general principles of treatment in which it occurs are admirable features, and some of the best chapters are those on bacterial resistance, on staphylococcal infections, and on tuberculosis. The last in particular is the most informative and readable general account of this highly specialized branch of chemotherapy which has yet appeared. The book can be recommended confidently as a guide both to principles and to practical therapeutics.

L. P. GARROD.

FAVOURITE PRESCRIPTIONS

Favourite Prescriptions. Edited by Sir Heneage Ogilvie, K.B.E., D.M., M.Ch., F.R.C.S., and William A. R. Thomson, M.D. 2nd edition. (Pp. 88. 5s.) London: The Practitioner. 1954.

The second edition of this book contains a good new chapter by Dr. Philip Evans on paediatric prescriptions. It is doubtful, however, whether this justifies the perpetuation of a work so often advocating complex and irrational mixtures which are both unnecessary and uneconomic. The *National Formulary* fulfils most prescribers' requirements much more efficiently. The doses are expressed in imperial measures, and, except in Dr. Evans's chapter, the metric equivalents are clumsy and pedantically precise. Much of the treatment recommended is out of date and ill-advised. It is doubtful, for instance, whether 15 to 30 minims of oral nikethamide taken night and morning, or a mixture of strychnine hydrochloride and dilute hydrochloric acid, will help "the elderly suffering from arteriosclerosis and low blood pressure and/or vascular lesions in the brain"; and the addition of ammonium bromide to an iron mixture is likely to exacerbate rather than to relieve the "dull headaches and depression" met with in anaemia. It is a pity that the all-too-common belief that the neuritic pains commonly encountered in this country can be relieved by aneurine hydrochloride should be perpetuated, and that bromides should continue to be given pride of place in the treatment of epilepsy. Medical students would rightly be reprimanded for following the advice to use oily drops in nasal conditions, intravenous potassium (without qualification) for infective hepatitis, and topical sulphonamides for burns. Such examples could be multiplied many times. The advent of powerful and specific modern remedies should make us reconsider the advisability of using many of the preparations advocated in this book. There is a place for the use of placebos in medicine—though they are dangerous drugs for the doctor who prescribes them—but it is doubtful whether a book which gives them such a prominent place is necessary or desirable.

D. M. DUNLOP.

THE ACUTE ABDOMEN

Diagnosis of Acute Abdominal Pain. By William Requarth, M.D. Foreword by Warren H. Cole, M.D. (Pp. 243; illustrated. 38s. or $5.) Chicago: Year Book Publishers, Inc. London: Interscience Publishers Ltd. 1953.

This is essentially a description of the surgery of the acute abdomen from the clinical standpoint. It is well illustrated by photographs, radiographs, and diagrams, and by clear descriptions of typical cases, and will reward careful study. Very full references to the literature will help those who want to make a special study of any one of the many different conditions described. To the student the elaborate laboratory tests described may be of interest, but we feel that they will be looked at a little askance by the practical surgeon—perhaps of the old and out-of-date school—who has dealt with many acute abdomens and often in the middle of the night.

To one who was taught by Henry Head and learnt at first hand his great work on visceral pain the book is a little disappointing, for it bears little relation to its title. There is no mention of the mechanism of abdominal pain or of what may be learnt from its study. Epigastric pain as an early symptom of appendicitis is mentioned, but not as indicating distension of the appendix; and the change in site and character of pain as infection reaches the lymphatics is not brought out. It is surely important to recognize the different characters and meaning of visceral pain, peritoneal pain, and referred pain, perhaps from the pleura, and to understand the mechanism of each. Apart from these small criticisms the book contains a large amount of useful information in small compass and is admirably produced, so that the excellent illustrations can be fully appreciated.

HENRY SOUTTAR.

MANAGEMENT OF PAIN

The Management of Pain: With Special Emphasis on the Use of Analgesic Block in Diagnosis, Prognosis, and Therapy. By John J. Bonica, M.D. (Pp. 1,533. 444 illustrations. £7 5s.) London: Henry Kimpton. 1953.

This book presents in one volume a complete discussion of the fundamental aspects of pain, the various diseases and disorders in which pain constitutes a major problem, and the methods employed in its management, with special emphasis on the use of analgesic block as an aid in diagnosis and treatment. The author is to be congratulated on the highly successful way in which he has covered this vast field. Numerous and detailed references are given at the end of each chapter, and these will prove of the greatest value to anyone seeking further information on a particular problem.

The book is composed of three parts: the first part includes a discussion of the fundamental aspects of pain, the author stressing that in order to manage pain properly its anatomical, physiological, and psychological bases must be understood. The second part is on the methods and techniques of managing pain, including not only analgesic block but also such subjects as the use of general analgesic methods, psychotherapy, physical therapy, and neurosurgery. Analgesic-block methods are discussed in great detail, and the account of them is one of the best yet published. The illustrations are excellent and the text is of remarkable clarity. Anaesthetists and others called upon to perform regional blocks for the management of painful conditions will find this section invaluable. In the third part the author presents the various diseases or disorders with painful syndromes which have been and can be managed with analgesic block with or without the aid of other methods.

Despite its size the subject-matter of this book is covered in a concise and readable fashion. The style of the text and layout of the book are most attractive; there are nearly 450 illustrations of excellent quality. This book is highly recommended to all interested in the management of conditions in which pain is prominent.

CYRIL F. SCURR.

BRITISH MEDICAL JOURNAL
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PROLONGED TREATMENT WITH CORTISONE AND A.C.T.H.

Much experience has been gained in the use of cortisone and A.C.T.H. in the five years since Hench and his colleagues[1] reported the remarkable remissions which could be produced by Kendall's Compound E in rheumatoid arthritis. Clinicians in the U.S.A. have had access to larger supplies of these substances and for a longer period than workers in this country, where both have been sparingly distributed by the Ministry of Health. As a result much of the available material has been devoted here to relatively short courses of treatment or used in topical therapy, and most of the reports on the results of prolonged treatment have emanated from abroad. In the last two or three years, however, enough has been distributed to enable studies to be carried out on several series of patients. No one who has seen the immediate effects of cortisone or A.C.T.H. can doubt that they bring about profound and dramatic improvement in a variety of serious disorders. Apart from Addison's disease and hypopituitarism, where they are rationally used as a form of replacement therapy, it cannot be claimed that they do more than suppress symptoms. It is true that in some conditions they may tide a patient over an acute phase until a natural remission occurs, and they have been likened to an asbestos suit which enables the wearer to remain unscathed in the flames until the fire has burnt itself out. Unfortunately far too often the fire remains alight, and it seems as if the victim is doomed permanently to wear this uncomfortable apparel.

Rheumatoid arthritis is by far the commonest of the diseases relieved by cortisone and A.C.T.H., and it will be long before there is enough of these drugs to treat every case. The original hope that short courses of treatment would give lasting benefit has proved unfounded, and it is now realized that when treatment is discontinued many cases relapse. Interest is thus directed towards the benefit which may reasonably be expected from indefinitely prolonged administration. It is, moreover, necessary to weigh this benefit against the side-effects and complications that may arise. Some of these are avoidable or reversible by manipulation of the dose, but others endanger life and have sometimes proved fatal. Opinions about the ultimate value of long-term therapy with cortisone in rheumatoid arthritis vary considerably. Most observers agree that it is often difficult to find a dose which will continue to relieve symptoms without giving rise to side-effects; all agree that advanced cases with ankylosed joints are unsuitable. But experience shows that in general patients are definitely better when they are receiving cortisone. It has, however, been claimed[2] that this improvement is no greater than can be achieved without the use of a potentially dangerous drug. This view receives strong support from a carefully planned and statistically controlled comparison of cortisone and aspirin in early cases of rheumatoid arthritis. This clinical trial, published in our opening pages this week, was sponsored by the Medical Research Council and the Nuffield Foundation; it was designed to answer a specific question: "Is it possible to maintain the well-being of a patient suffering from early and uncomplicated rheumatoid arthritis as well with aspirin as with cortisone?" Somewhat surprisingly the answer is unequivocally Yes.

In this series of sixty-one patients two comparable groups were treated and observed for a year. Great care was taken to ensure that the cases were matched with regard to sex, age, and duration of symptoms. The sheep-cell agglutination test gave confirmatory evidence of the accuracy of the diagnosis. Observations were made on the patients' general functional capacity and the activity of the disease. Measurements were carried out on strength of grip, on range of movement of the wrist, and on dexterity of hand and foot. Joint tenderness was assessed and the haemoglobin level and erythrocyte sedimentation rate determined. Standard doses of both drugs were used during the first fortnight, but later the quantities were adjusted for each patient so that a balance was maintained between benefit and side-effects. This dose was quite high, with a mean value of 76 mg. a day of cortisone (range 25–125 mg.) and 4.5 g. a day of aspirin (range 1.7 to 6.0 g.). The aspirin was camouflaged in brown tablets with a bitter flavour, and it seems unlikely that patients recognized the nature of these "Tabs. Rheumatic C." The results were statistically analysed by Dr. J. T. Boyd, of the Medical Research Council, but so similar was the progress of the two groups that simple inspection of the tables is convincing enough evidence of the validity of the deductions. The cortisone group had significantly higher haemoglobin levels and lower sedimentation rates than the aspirin group at the end of a year's treatment, but the differences were small. Perhaps the most important fact revealed by the investigation is that in 75% of the patients treated by aspirin

[1] *Proc. Mayo Clin.*, 1949, **24**, 181.
[2] West, H. F., and Newns, G. R., *Lancet*, 1953, **2**, 1123.
[3] Ibid., 1948, **2**, 771.
[4] Smith, M. J. H., Gray, C. H., and Lunnon, J. B., ibid., 1954, **1**, 1008.
[5] Bayliss, R. I. S., and Steinbeck, A. W., ibid., 1954, **1**, 1010.
[6] *British Medical Journal*, 1954, **1**, 1109.
[7] Ibid., 1954, **1**, 1205.
[8] Ibid., 1954, **1**, 1171.

the disease was judged to be inactive at the end of a year and that 40% were capable of normal work and activity. It is by this standard that other forms of therapy must be assessed. It is interesting to speculate on the degree of improvement which might have been achieved if it had been possible to treat a similar group of patients with inert tablets or with some other analgesic such as phenacetin. Possibly what is being observed is the natural progress of the disease rather than the specific effect of a salicylate; nor can the element of suggestion be entirely excluded. Asher[3] showed that inert tablets relieve pain in 50% of administrations, partly through suggestion and partly because they may be given at a time when pain is remitting spontaneously. Moreover, it cannot now be claimed that aspirin exerts its effects by stimulating the anterior lobe of the pituitary or the adrenal cortex, since salicylates do not increase the excretion of adrenocortical steroids[4] or raise the plasma level of 17-hydroxycorticosteroids.[5]

Dr. W. S. C. Copeman and his collaborators,[6] in a paper published in this *Journal* a fortnight ago, approached the problem of prolonged therapy of rheumatoid arthritis with cortisone from a rather different point of view. They reported the results of at least a year's treatment of twenty incapacitated patients, of whom seventeen had been able to return to their occupations. They were all severe cases of at least two and a half years' standing and described themselves as "crippled." They had received previous treatment with salicylates and gold salts, though no details of the extent of the courses were given. The average maintenance dose in this series was 69 mg. of cortisone a day. These observers believe the most suitable patients for cortisone treatment are those in whom functional disability exceeds the anatomical joint damage. Dr. F. Dudley Hart and his co-workers[7] have also recorded the effects of cortisone treatment in doses of 25 to 75 mg. a day on twenty-two cases for six to eighteen months with "satisfactory" results in thirteen, "unsatisfactory" in four, and "unchanged" in five. They make the point that those showing a prompt reduction in soft tissue swelling benefit most, and conclude that cortisone therapy is a valuable addition to existing methods, even if it helps only a small proportion of sufferers.

In comparing these somewhat conflicting views it should be noted that the cases reported in this issue by the joint committee were all early and relatively mild. It may well be true that different results would have been obtained if long-standing and crippled cases had been included. But it will in future be necessary to determine the effects of full doses of aspirin before claiming that cortisone gives better results. It might be possible to devise some sort of cross-over test in which the individual patient could act as his own control, and no doubt observations on these lines will be made. One important difference between cortisone and aspirin is the nature and severity of the toxic effects to which they give rise. Copeman and his colleagues divide them conveniently into those which are dangerous to life and the less important side-effects. Of their twenty patients, one developed psychological disturbance and one hypertension sufficiently severe to require withdrawal of the drug, and peptic ulceration was diagnosed in three and diabetes mellitus in one. In the joint committee's series side-effects were relatively mild and were equal in the early months of treatment with both aspirin and cortisone, but became less in the aspirin group as time passed. It must be admitted, however, that aspirin administration in full doses, though it may lead to unpleasant side-effects, is unlikely to endanger life and is greatly preferable to cortisone from this point of view.

If further experience confirms the view that most cases of rheumatoid arthritis can be treated as effectively and more safely with aspirin than with cortisone, larger quantities of cortisone will be available for the maintenance therapy of other conditions. The results of long-term steroid therapy over two and a half years at Guy's Hospital are therefore of special interest. Last week in this *Journal* Drs. E. H. McGehee and K. MacLean[8] list the diagnoses of 185 cases treated with A.C.T.H. and cortisone and describe their experience of prolonged therapy of twenty-six cases of "collagen" diseases, skin disease, and eye conditions. In general the results they describe are more satisfactory than in most reported series. Many patients entered a phase of remission. Of special interest is their account of intermittent therapy with A.C.T.H. gel, which enables patients to attend hospital for review at only weekly or bi-weekly intervals. Complications which were encountered included three cases of gastro-intestinal perforation with two deaths, three psychotic episodes, and one case of diabetes.

Cortisone and A.C.T.H. are substances of outstanding physiological and pharmacological interest. At first, high hopes were held that we had in our hands the clue to the mechanism of many obscure diseases and that we could give sufferers from them permanent relief. This prospect is fading rapidly, and we can do little more than suppress symptoms and hope that the patient will undergo a natural remission and will not suffer a serious complication from the drugs he is receiving. Most of these diseases are in any event rare. It will be ironical if the major practical outcome of all the intensive work of the last few years is the discovery that aspirin given in maximum tolerated doses is the best and safest treatment for rheumatoid arthritis, the only common disorder for which cortisone is used.

VIRULENCE IN VIRUS DISEASE

What matters about viruses, so far as man is concerned, is their virulence; and to combat virulence an absolute understanding is needed of the complex set of factors which determine it. This is the basis of the experimental approach to the problem of virulence in virus disease—the subject of the Ciba Foundation Lecture recently given by Sir Macfarlane Burnet in London. Virulence is shown by the capacity of a virus to produce recognizable disease with lesions, symptoms, or death in a given host. The virologist attempts to show this when trying to establish a virus to grow in a new host; and it must be remembered that virulence will be determined not only by the virus but by the susceptibility of the host. In some cases several passages may be necessary before changes indicating cell damage of some magnitude are obtained. When this happens the virus concerned will be regarded as one of high virulence. Many viruses exist in nature as inapparent infections, multiplying probably at a slower rate and producing less obvious changes. Similarly in the laboratory there are many viruses, such as influenza and mumps, well adapted to growth in a particular medium, which produce little or no recognizable cell damage. Therefore, according to the particular virus–cell system being studied, marked variation in degree of virulence must be expected both in nature and in the laboratory.

The assessment of virulence in terms of quantity of virus is technically difficult. Direct counting of virus particles by electron microscopy is not yet a practical procedure. Similarly, histological examination is only of value in a virus–cell system where specific changes can be seen. The capacity of influenza and certain other viruses, including mumps and Newcastle disease virus, to agglutinate red cells affords a new approach to the quantitative estimation of virus. Under standard conditions haemagglutinin titrations present a simple and accurate *in vitro* test for estimating the concentration of virus in a given suspension, irrespective of its degree of virulence.

In the last few years Burnet and his team in Melbourne have been investigating the virulence of different strains of influenza virus, using the chick embryo for culture and the haemagglutinin test for titration. Most influenza A strains, which on primary isolation from a human case grow well in the chick embryo, produce little change in the mouse lung, apart from minor toxic effects; virus multiplication, however, occurs, and at about the eighth passage first signs of pulmonary consolidation develop. By the twentieth passage the mice succumb regularly with complete consolidation of the lungs. Examination of the original virus (which was avirulent for the mouse) and the final virulent material in the neutral medium of the chick embryo shows that the only significant difference between the two is their relative virulence for the mouse lung. With the standard technique of limit dilutions employed in this work it seems clear that virulence is a genetically determined factor. Analysis of the bronchial washings taken from mice at different stages of the development of pulmonary consolidation and tested by the same method of limit dilutions strongly suggests that the increase in virulence is due to the selective survival of increasingly virulent mutants.

Under certain conditions, when two strains of influenza virus dissimilar in virulence are allowed to infect the same host, recombination of virus occurs, and the progeny of the double infection may have individual characteristics of the two parent strains.[1] In an extensive series of experiments Burnet and Lind[2] have shown that when a virulent and a non-virulent strain are crossed, strains of varying degree of virulence will emerge in the redistribution of virulence which results from genetic interaction. Burnet considers that in the same way the gradual development of virulence seen in the adaptation of influenza A strains to the mouse lung results from multiple genetic interaction and suggests that virulence genes exist as part of the virus make-up.

This work has a bearing on methods of controlling virulence in virus disease. Active immunization against yellow-fever, for instance, has been made possible by reducing the virulence of the live virus in the vaccine by a process of attenuation. The control of poliomyelitis by active immunization may well require in the long run the use of an attenuated virus vaccine: to achieve this will demand a very clear understanding of all the factors that govern virulence. Burnet's work with the influenza virus has been possible because of the ease with which the virus can be handled in the laboratory. It remains to be seen whether the study of other animal viruses can be approached in the same way. From the practical standpoint it will be difficult, but this important contribution from the Australian workers will undoubtedly arouse great interest and direct attention to the problem of virulence in virus disease as a whole.

[1] Burnet, F. M., and Lind, P. E. (1950). *J. gen. Microbiol.*, **5**, 60.
[2] —— —— (1954). *Nature, Lond.*, **173**, 627.

AMERICAN SURGEONS IN LONDON

Apart from their purely professional value, international medical congresses can do much to promote sympathy and understanding between the nations. This function could nowhere be better exemplified than at the sectional meeting of the American College of Surgeons which was held in London for three days last week. A large number of American, British, and other surgeons gathered together on this

occasion. Before their arrival in London many of the Americans had already attended meetings in Glasgow and Edinburgh, as well as the annual meeting in Leeds of the Association of Surgeons of Great Britain and Ireland. As if this programme was not enough for them, some of our visitors went on immediately to meetings in France, Belgium, and Italy. In London the surgeons have chiefly forgathered at Lincoln's Inn Fields, and the occasion proved a fitting inauguration for the beautiful new Great Hall of the Royal College of Surgeons, completed only a few weeks ago. Although other parts of the College were also used for the various discussions, the huge hall, with its English chestnut panelling, gurjun floor, and power-driven window-blinds, was the centre of attraction. Adjacent to this, and used for a number of social occasions during the meetings, is the new council chamber, which has oak veneer panelling—presented to the College by Ethicon Suture Laboratories Ltd—from a single tree planted at Lilford Park, Northamptonshire, in the reign of Elizabeth I.

The scientific programme was unusually full and varied. Each morning from 9 to 12 o'clock there was a marathon of papers, and many of these were presented in pairs, the opening speaker having twenty minutes and the second speaker ten. These paired papers were in each instance presented by an American and a British surgeon, and the time limit was strictly enforced. This intensive method of presentation of so many papers in the course of a morning was sometimes rather overpowering for the listener; but, after experience of so many British medical meetings, where time control is lax, those who were present could not but admire the way in which speakers were made to adhere to the timetable. Among such a large number of papers it would be invidious to single out individual contributions, most of which are referred to in this or in our last issue. But of particular note was Sir Gordon Gordon-Taylor's remark that he had performed his seventy-first hindquarter amputation on his 76th birthday. Enjoyable variations from the ordinary run of meetings were the two luncheon discussions at the Connaught Rooms. At each of these gatherings a panel of four speakers and a moderator dealt with the chosen subject in the space of one hour. Once again it was good to see the efficient organization, and the way in which the main speakers were encouraged to be brief, informative, and to the point. Supplementary questions, written out by members of the audience, were selected and presented by the moderator, this task being undertaken by Mr. Dickson Wright for a discussion on intestinal obstruction, and by Dr. Frank Glenn, acting president of the American College of Surgeons, for one on massive haemorrhage from the gastro-intestinal tract. Dr. Glenn's breezy, incisive, and expert cross-examination of the members of his panel kept them all on their toes and enhanced the value of a lively and helpful discussion.

In addition to the formal papers and luncheon discussions, visits were made to a large number of London hospitals where a variety of interests was catered for in the clinical and operative demonstrations which had been arranged. The presentation of a Hunterian Lecture by a surgeon from the United States and of a Moynihan Lecture by a Canadian, further panel discussions on pre- and post-operative care and on hand surgery, as well as other meetings for those specially interested in gynaecology, ophthalmology, oto-rhino-laryngology, and urology, all served to emphasize the catholicity of this gathering. Apart from this intensive professional programme, the social side of the meeting was so full as to tax the endurance of the keenest socialite. Receptions were held at Lancaster House on behalf of Her Majesty's Governmen, at the House of Lords, the Society of Apothecaries, and the Ciba Foundation, as well as the Royal College of Surgeons. Suitable entertainments were arranged for the ladies, and on the second night there was a banquet at the Dorchester Hotel which was attended by 850 surgeons, their wives, and guests. Dr. Fred W. Rankin, president of the American College of Surgeons, the news of whose death on May 22 will have saddened his many friends in this country and elsewhere, was to have presided, and Dr. Frank Glenn took his place. The toast of the two Colleges was proposed by the Marquis of Salisbury and acknowleged by Dr. Glenn and Sir Cecil Wakeley, P.R.C.S. The whole meeting was widely adjudged a great success and a delightful example of international co-operation of the best possible kind. At the present level of medical incomes, drastic taxation, and sparse dollar allowances, probably not more than a handful of British surgeons could manage to travel to the United States for a similar congress. Perhaps better days will come, and meanwhile all will be grateful to our American friends for coming over here in such large numbers.

ROYAL SOCIETY CONVERSAZIONE

The song of cicadas buzzing at the Royal Society's conversazione last week may have reminded some of the Fellows of their less intellectual evenings by vineyard or beach, but it served here to reveal the physiology of its production under the guidance of Mr. J. W. S. Pringle, F.R.S., of Cambridge. Near by, that humbler insect the housefly was on show, strains resistant to insecticides being displayed in jars by Dr. R. Busvine, of the London School of Hygiene and Tropical Medicine A few strains resistant to D.D.T. have now been found in England. Also from this school came another exhibit of insects: Dr. K. Mellanby showed how they can be rapidly acclimatized to normally lethal temperatures if they are first kept for a short time at an intermediate

temperature. Mr. A. F. Huxley, of Cambridge, showed an interference microscope, an instrument that has some advantages over the phase-contrast microscope, one being that it gives a more faithful image. Another ingenious piece of microscopy was being demonstrated by Sir Geoffrey Taylor, F.R.S., and Lord Rothschild, F.R.S., also from Cambridge. They had bulls' spermatozoa swimming in water and illuminated in the microscope field by a rapidly interrupted light. By adjusting the rate of interruption, the tail of any particular spermatozoon could be made to appear motionless even though it was flickering rapidly. The various types of oxygen equipment used in the climbing of Everest last year made an unusual exhibit. Inevitably rather heavy and cumbersome, their display served to remind visitors, albeit unwittingly, of the human will and muscle that were as necessary as inventive skill for living at those heights. Physiology of a kind more reminiscent of student days came from Mr. J. E. Pascoe, of the Physiology Department of University College, London, who showed how changes of temperature alter the transmission of impulses through an isolated nerve ganglion, and from Mr. A. C. Downing and others, of the same department, who showed how changes of pressure alter the contraction of an isolated frog muscle.

Once again the Marine Biological Association of the United Kingdom had dredged from the sea a variety of starfish, sea squirts, worms, and crustacea. Some of these animals, with their highly coloured integuments, owe their brilliant pigments to their ability to concentrate such rare metals as niobium and vanadium from the sea-water passing through them. That Nature still outstrips Man in inventiveness seemed to be the lesson that this exhibit bore for the radar experts in the next room.

CONFERENCE OF HONORARY SECRETARIES

In this week's *Supplement* (p. 283) we report the proceedings of this year's conference of Honorary Secretaries of Divisions and Branches, which took place at B.M.A. House on May 19, with Dr. D. M. Hughes in the chair. This annual event is an important one in the Association's calendar. It enables honorary secretaries from all over the United Kingdom to get together in a not too formal atmosphere and to pool the resources of their wide experience in furthering the smooth working of the organization. Not the least valuable part of the Conference is the opportunity which it gives for making personal acquaintances between the secretaries in the periphery and the Headquarters staff.

Mr. H. H. Langston, who is chairman of the Constitution Committee, recently set up by the Council to review the Association's organization, spoke in the morning on the question of "What is the most effective area as the basic unit of the Association?" and left no doubt that in his view it was the Division—a view which was supported in the discussion which followed. It emerged that the majority present felt that a small Division had more chance of fulfilling its function actively than a large one, and that the friendly spirit was more readily evoked among a small number. The afternoon session brought suggestions from Dr. V. Cotton Cornwall on how the Association in its Divisions and Branches could help the newly qualified hospital resident, and Dr. Joan Chappell, who followed, thought that the Divisional meeting should be the Association's local shop-window and should show itself to the hospital resident as worthy of more than a glance. In the general discussion it was clear that honorary secretaries fully realized the need to attract and to help the young doctor, and many gave useful accounts of what they were already doing in this direction.

THE PRESIDENT'S TOUR

Last week the President, Mr. Tudor Thomas, gave a full report to the Overseas Committee on his recent tour on behalf of the Association of its Branches and Divisions in the Middle and Far East. The object of the tour was to carry greetings and good wishes from the Association in the United Kingdom to its members in these places, to express an interest in their welfare, and to help them in any way possible. It is not always realized that the B.M.A. has responsibilities towards some 4,000 members in Branches scattered over many countries outside the British Isles, not to mention the 11,000 in the Branches in Australia and New Zealand. The President was able to visit only five Branches, representing some 1,500 members, but they are perhaps among the most isolated by distance from contact with Headquarters in London, and barred by geographical obstacles from frequent meetings of members within their own bounds. The 150 members of the Middle East Branch, for instance, are spread over seven countries.

Mr. Tudor Thomas, accompanied by Mrs. Tudor Thomas, left London on March 9 and returned on April 24, having travelled in the interval some 22,500 miles by air and reaching as far east as Hong Kong. But this feat, formidable in itself, was, so to speak, only the connective tissue of a programme of some 30 addresses and lectures, a broadcast, 50 official dinners, lunches, and receptions, and visits to over 30 hospitals (where patients were often seen in consultation) and university departments. These figures speak for themselves of the amount of official business that was got through, but they do not record those numerous personal contacts which are the essence of such a tour, and to the value of which the President refers as follows: "Many of the doctors whom I met had never been in England and had never seen the workings of the Association in this country. I felt that they were pleased to realize that they formed part of the Association and that by my visit they were perhaps making a closer contact with the Association than they had ever done before." That the journey fulfilled its object in every way is clear from the President's modestly phrased report, and in thanking him for undertaking this strenuous task the Association will be conscious of its good fortune in having at its service so able an ambassador. All who know Mr. and Mrs. Tudor Thomas will be sure that, wherever they went, they left behind them a greater understanding of the functions and traditions of the B.M.A. and an enhancement of its prestige.

CLINICAL PATHOLOGY IN GENERAL PRACTICE

BIOPSIES

BY

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A biopsy is an examination of tissue removed surgically. Since the term "biopsy" implies an examination, it is superfluous to speak of "biopsy examination." When the surgeon says he is "taking a biopsy," he is in fact "taking a specimen for biopsy" or "taking a biopsy specimen"; biopsies are performed by the pathologist, not by the surgeon, who simply obtains the material. Another name for this branch of pathological work is "surgical histology," which indicates clearly both the source of the material and the characteristic feature of the examination. The term "histopathology" has no advantage over "biopsy" and "surgical histology," and does not indicate whether the material was obtained from the living or the dead.

Biopsy may be performed before, during, or after treatment of the patient. When the lesion is both large and readily accessible—for example, on the surface of the body or in the mouth or rectum—the surgeon may remove a small piece of it and await the pathologist's report before deciding on the treatment. A lesion that is both small and readily accessible should be excised completely; there is no point in subjecting the patient to two operations; one, an excision of a minute fragment of the lesion for pathological diagnosis, and the other, excision of the rest of the lesion. Surgical excision of a lesion is preferable to therapeutic destruction of it *in situ*, since excision allows of a microscopical examination. When the diagnosis is reasonably certain on clinical grounds—for example, if the patient has the usual signs of a mammary scirrhus—the surgeon treats the patient radically without preliminary biopsy in the confident expectation that the diagnosis will be subsequently confirmed by the pathologist. When the lesion is internal, preliminary biopsy is often impracticable, and the biopsy can be made only on the specimen obtained after treatment on the strength of the clinical findings.

Value of Biopsy

All material removed surgically is worth examining, no matter how sure of his diagnosis the surgeon may feel. Although the clinical diagnosis is often confirmed, surprises are not rare, and the prognosis or treatment may be radically revised as the result of the pathologist's report. Malignancy may be simulated exactly by benign conditions; familiar examples are certain inflammations of the large intestine; and giant hypertrophic gastritis, though rare, may be clinically indistinguishable from gastric cancer. Conversely, lesions that the surgeon thinks benign—in the breast, for instance—may prove on microscopical examination to be malignant.

The certainty of pathological diagnosis varies as widely as that of clinical diagnosis. Many diseases are identifiable with certainty on examination of a section; these include most surgically removed cancers and tuberculosis and other well-known infections. Sometimes only the general nature of the disease is determinable; for example, a malignant growth may be so undifferentiated as to be unclassifiable even broadly as carcinoma or sarcoma, but the fact of malignancy is nevertheless an important item of information. Sometimes the same histological picture is given by different diseases; in some cases of Hodgkin's disease the lesion is microscopically identical with that of mixed-cell sarcoma, and the two conditions have probably been confused. Similarly, early Hodgkin's disease in a lymph node may be microscopically indistinguishable from lymphatic leukaemia or lymphosarcoma. Some clinically malignant tumours may show little or no histological evidence of malignancy; these include certain "myxomas," "lipomas," and tumours of the thyroid; in such cases treatment must obviously be based on the clinical findings, supplemented when practicable by examinations other than biopsy.

The Specimen

The sooner a specimen is fixed, the better the section will be; the specimen should therefore be put in a fixing fluid immediately after its removal from the body; if the fresh specimen is put aside in a dish to be dealt with at the end of the day's operating, it may easily be thrown away or be left to dry until the hatching of maggots reminds someone of its presence.

The best practice is for the laboratory to keep the operating theatres supplied with vessels of various sizes already containing the fixative. The most convenient fixative is 10% formol saline; a litre of this consists of 100 ml. of commercial formalin, 900 ml. of tap-water, and 8.5 g. of sodium chloride. Since commercial formalin is a 40% solution of formaldehyde, the fixative contains 4% formaldehyde. Owing to the similarity of their names, formol saline and normal saline could be confused, with serious results; it would therefore be best if each container bore a large coloured label with the words "Pathological Fixative—Poison."

The whole of the tissue removed should be sent to the laboratory. This enables the pathologist to see the lesion as a whole, to note its relation to surrounding tissues, and to choose the best points for sampling. The whole of an amputated limb is not often sent, but if the condition is serious enough to require amputation the pathologist ought to have the whole limb so that he can study the extent of the tumour or the state of the blood vessels. To deal satisfactorily with large specimens such as limbs or massive tumours, the pathologist needs the help of the surgeon; by examining such specimens together, they can decide on the most suitable parts for microscopical examination, and so obviate the necessity for cutting many blocks. It is not unknown for the laboratory to receive only a minute fragment of a large excised tumour, or even only tissue adjoining an excised tumour, because the tumour itself was wanted for somebody's private collection. The commonest mistake of the surgeon is to send a part when he should send the whole.

When the specimen is more than a few inches in diameter, the surgeon should bisect it through the part containing the lesion. This gives the fixative immediate access to the lesion and incidentally allows the surgeon to see at once what he has removed. The worst fault is to make multiple incisions into such specimens as lymph nodes and small tumours of the breast; in such cases it may be impossible to get a satisfactory section for microscopical examination. Another good reason for not incising lymph nodes is that they may be heavily infected; they should be allowed to fix for some time before being opened.

Urgent Specimens and Dispatch

When a request form is marked "urgent" the time normally needed for reporting is reduced by (1) processing faster than usual if the specimen is small, (2) examining the section as soon as it is ready, and (3) telephoning the report. Abnormally rapid processing may result in poor sections, and consequently the diagnosis may be difficult or impossible; extra tissue may then have to be processed, the final result being a longer delay in reporting than if the request had not been marked "urgent." It is not desirable to process lymph nodes faster than normal, although time can be saved by immediate examination and telephoning the report.

There may be a variety of good reasons for "urgent" requests, but such requests should be made with discretion, and preferably with an explanation of the nature of the urgency. The laboratory has equal obligations to many surgeons, and every "urgent" request from one surgeon means delay in reporting for others. Most surgeons in fact make "urgent" requests only at long intervals, and the requests are accordingly accepted without question; when "urgent" requests come in large numbers from a single firm, the pathologist may well suspect that the word "urgent" is being used with insufficient discrimination.

A specimen for examination deserves at least the same care as a registered letter. There is little or no risk of loss once the specimen has been collected from the operating theatre by the messenger; but loss and delay are familiar enough in the theatre. The trouble is that usually no one is responsible for seeing that specimens are dispatched promptly and properly. The surgeon may ask the theatre sister to send them, but she may well pass on the instruction to another nurse or orderly—and either may have gone off duty when the messenger arrives to collect the day's specimens.

One person should be made responsible for the dispatch of specimens, and the most suitable person is the surgeon's assistant, who knows the importance of pathological examinations and what the requirements are; no member of the nursing staff is properly qualified for this function. The assistant in charge of specimens should never delegate his responsibility, but see to it personally that the specimens are collected by the messenger. There should be no difficulty in fixing regular times for the collection of specimens.

Data Needed by Pathologist

The meaning of a histological picture sometimes depends on the patient's age and the history of the lesion; if the pathologist is not informed of these, he can easily make a wrong diagnosis. A familiar example is the pigmented mole of the skin; this may look particularly malignant under the microscope and a report in this sense might result in an amputation. In childhood such moles are usually benign, however malignant they may look, and inquiry may show that the lesion has been present for years without any increase in size.

The accumulated experience of pathologists finds expression in the blank form commonly supplied to the surgeon who wants a specimen examined. This form requests such obvious particulars as the patient's name, sex, age, and ward; the site of the lesion; the duration of the illness; the clinical diagnosis; and the treatment given, especially if it is likely to affect the microscopical appearances, as in toxic goitre. This represents the bare minimum of information needed by the pathologist before he can form a sound opinion. All the information asked for by the laboratory should be supplied, preferably by the surgeon himself and not by an assistant or nurse.

The printed form cannot provide for all the information sometimes required by the pathologist. In specially difficult or interesting cases the surgeon may realize this and anticipate the need by sending unusually detailed information, but the pathologist often has to extract the information himself from the surgeon or his staff. When full information has been supplied, it is sometimes possible for the pathologist to suggest a likely diagnosis from this alone.

Whenever there is doubt or difficulty on either side, surgeon and pathologist should meet for discussion. Such consultations usually result in complete agreement on the most probable diagnosis and the most suitable treatment and are of immense benefit to the patient; some surgeons are well aware of this and consult regularly. At the other extreme we have the surgeon who goes in for "penny-in-the-slot" pathology; consulting, usually with the reporter's superior, only when a mistake has been made through the surgeon's failure to supply essential information; or seeking a second opinion on a section without the knowledge of the reporter. A competent pathologist knows when he ought to consult a fellow-pathologist, and, the more able he is, the more often he sees the need and consults. Any query about a report should of course be raised with the reporter, not with a third party.

Paraffin and Frozen Sections

Paraffin sections are normally used for diagnostic purposes; the sections are stained with haemalum and eosin or some other routine combination of dyes. The introduction of automatic tissue processers has greatly reduced the minimum time interval between receipt of the specimen and issue of the report. The normal interval is now from two to three days, but very small specimens, such as those from a bronchus, can be processed and reported on within a day of receipt. These periods are attainable only if the section is of satisfactory quality and the microscopical diagnosis obvious. The chief cause of delay in reporting is difficulty in diagnosis; this may call for staining of further sections by special methods, the making of extra blocks, consultation with the surgeon or another pathologist, or work in the library. In such cases it may be possible to issue a provisional report.

The advantage of frozen sections is that they can be made within a few minutes of receiving the material, and where special arrangements exist the surgeon can interrupt the operation until he receives the report. The disadvantage is that frozen sections are much less satisfactory for diagnostic purposes than paraffin sections. When the surgeon is reasonably certain of the diagnosis on clinical grounds, he sends the specimen for examination by the paraffin method after the operation; it is when he is in serious doubt, having begun the operation, that he would most like a report before proceeding. But when the surgeon finds it difficult to make a diagnosis, the pathologist often does so too, and finds it more than ever necessary to study a paraffin section before expressing any opinion. When a biopsy is not feasible before operation, the surgeon should normally act solely on the clinical data, without interrupting the operation for a frozen section to be made, and send the specimen afterwards for study in a paraffin section. An exception to this rule may be made by the neurosurgeon, since frozen sections of tissue (or squashes of tissue) obtained by needling during an operation may enable the pathologist to say whether a lesion is in fact a tumour. Work of this kind presupposes both special arrangements and special training in neuropathology and is therefore outside the scope of the general pathologist.

Cytodiagnosis

This means diagnosis from the appearance of isolated cells in such material as sputum, gastric contents, or uterine smears. The method is used chiefly for the diagnosis of malignancy. Its use has been advocated enthusiastically and perhaps uncritically, with the result that experienced pathologists often refuse to use the method at all or use it with considerable reservations. It is true that no preparation can compare with a good paraffin section of a piece of tissue for quality and reliability for diagnostic purposes. The pathologist who decides to use only such material ought not to be labelled conservative or out of date; he is, after all, thinking only of the best interests of the patient, and if he himself were the patient he would wish to be examined in the same way.

The one field in which cytodiagnosis is of proved value is that of gynaecology. Smears critically studied may be helpful in detecting early cancers of the cervix. It is not so much isolated atypical cells that are significant as the occurrence of atypical cells in large numbers; the preparation can then be regarded almost as a teased tissue, and the method does not differ radically from the examination of a section.

Cytodiagnosis has also been much used for the detection of bronchial carcinoma. I have examined many specimens of sputum for this purpose but have never been able to make a confident diagnosis of malignancy. Since the thoracic surgeon can often obtain a piece of tissue without much difficulty, and since malignancy can often be diagnosed with certainty even in a minute fragment of material, it is uneconomic to consume the time of technicians and pathologists in innumerable sputum examinations yielding negative or inconclusive results. The average pathological laboratory is already fully occupied with ordinary biopsies; if a routine cytodiagnosis service is required in addition, the hospitals will have to provide extra facilities, technicians, and pathologists, and to pay for the special training required—expenses that are certainly not warranted by the results obtainable.

Grading of Tumours

The pathologist is sometimes asked to grade tumours numerically according to the degree of their structural difference from the corresponding normal tissue. There is undoubtedly an infinite series of gradations in appearance between a normal tissue—epithelial or connective—and the most undifferentiated tumour derived from it, but so many factors other than tumour pattern may affect prognosis that the value of such grading is limited. Another difficulty is that we can usually examine only a small part of a tumour; the more tissue we examine, the clearer it becomes that there are often wide variations in the appearance of a tumour from point to point, even transcending the limits of recognized types. For example, a bronchial carcinoma, if thoroughly examined, may show features of several distinct varieties of this growth; estimates of the frequency of different varieties may thus depend on the extent of the examination. These remarks are equally true of carcinomas of the breast, and malignant tumours in general may be justifiably classified only according to the predominant pattern. While formal grading is not worth doing, the information of interest to the surgeon can be conveyed by skilful description in the pathologist's report, and more usefully, since the meaning of the report will be clear to all who may read it, and not only to those acquainted with a particular classification. A description of a tumour implies an assessment of the degree of malignancy, so far as this can be judged histologically; in this sense, tumours always have been graded by all competent pathologists for generations past.

Biopsy Reports

The object of a report is to help the surgeon, a fact that cannot be too often remembered by the pathologist. The writing of reports is an art that can be acquired only by practice, but some general principles are worth stating. The surgeon is busy: therefore reports should be brief. With many reports about many patients converging on him, he is not going to read a technical dissertation, without a heading, filling a page with single-spaced type. Every report should be headed by the diagnosis in two or three underlined words, and the text should normally require only a few lines of type, which should be double-spaced. The three or four salient points about a section can be got into such a report. When the result of the examination bears on prognosis or treatment, the report should make this clear; in particular, the pathologist ought not to leave the surgeon guessing whether he should perform a radical or conservative operation or no operation at all. When the pathologist himself is doubtful, he should discuss the case with the surgeon before writing the report; a short conversation often solves such problems. While a report must be truthful, it should also be tactful, so that an intelligent patient would not be unduly alarmed.

A rare or interesting lesion may call for an unusually full description, but long reports issued as a routine on all cases mean that the pathologist is incapable of selecting the salient points or of writing concise English. The worst possible reports are those that wobble helplessly between "benign" and "malignant," or consist of academic descriptions of phenomena from which no practical conclusion can be drawn. Most of us have probably written reports of this kind, but we learn in time to resolve our difficulties beforehand by consulting a fellow-pathologist.

Next article on Clinical Pathology.—"Tests of Gastric Function," by Dr. F. Avery Jones.

Refresher Course Book.—The first collection of articles in the Refresher Course for General Practitioners (fully revised) are available as a book containing 55 chapters, price 25s. Copies can be obtained either direct from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1, or from booksellers.

AMERICAN SURGEONS IN LONDON

CONCLUSION OF SECTIONAL MEETING

The sectional meeting in London of the American College of Surgeons concluded on May 19. The report of the first day's proceedings was published last week (p. 1203). During the three days of the meeting 64 papers were read, 32 by American and 32 by British authors. The meeting on May 18, presided over by Dr. F. A. COLLIER (Michigan), took the form of a symposium on cancer.

Cancer of the Lung and Cigarette Smoking

Professor E. A. GRAHAM (St. Louis) presented the results of a survey of 600 patients with cancer of the lung. A questionary was devised for the purpose of finding out how far cigarette smoking was implicated, and each patient was asked the questions at an interview. The results were nearly identical with those brought forward by Professor Bradford Hill and Dr. Richard Doll in this country. A remarkable relationship between excessive cigarette smoking and lung cancer was demonstrated, and the same was true of six additional studies carried out in the States. Atmospheric pollution had been advanced as an alternative cause, but this would not explain the sex incidence. The disease was five or six times as prevalent in men as in women. Any carcinogenic agent in the atmosphere would affect both sexes equally. On the other hand, it took 20 or 30 years of cigarette smoking to establish cancer, and large numbers of women had not been smoking for that length of time.

Mr. HOLMES SELLORS (London) described the results of surgical treatment of cancer of the lung. There were two methods of treatment available: the surgery of excision and radiotherapy. Results with the latter had been unfavourable, though the picture might be different with improved technique and apparatus. Age was not necessarily a contraindication to surgical excision; he had operated on many patients in their seventies, and his oldest patient was 84. He showed a table of results of 700 cases from three hospitals. At the end of two years after operation the proportion of survivors was 45%; after three years, 30%; after four years, 22%; and after five years, 20%. The most favourable type of cancer for operation was the medium-sized central squamous-celled carcinoma; 72% of the patients were alive after three years, whereas with "oat-celled" cancer the figure was 40%.

Cancer of the Thyroid

Mr. GEOFFREY KEYNES (London) opened the subject of cancer of the thyroid, giving the history of three patients. He discussed the value of radioactive isotopes. Professor WARREN COLE (Chicago) said that in the experience of his clinic the proportion of thyroid disease amongst patients admitted to the surgical wards was 15% in 1927. The figure had fallen to 10% in 1943, when thiouracil came into use, and was less than 5% in 1952. Non-toxic nodular goitre, however, had risen in incidence. The average age for the development of this condition was 44.5 years, and for carcinoma, 47.3 years.

Cancer of the Colon

Dr. ARTHUR W. ALLEN (Boston) spoke on the trend of treatment in carcinoma of the colon. Public health statistics in the United States showed in 1951 23,517 deaths from cancer of the colon (15.4% of all deaths from cancer), and 10,103 deaths from cancer of the rectum (6.6%). He discussed 316 cases on which he had operated from 1943 to 1954. In these, resection for cure was carried out in 256, and palliative resection in 49, accounting for 96.5% of the total; 11 (3.5%) were non-resectable. 182 of the patients had survived for five or more years. The operative mortality in these cases treated between 1943 to 1954 was only 4.3%, whereas in an earlier series, from 1925 to 1942, it had been 17.5%. With palliative resection the shortest survival time was one month (local spread from the sigmoid), and the longest 4.5 years (liver metastases from splenic flexure). The average survival time was nine months. With resections for cure the longest survival time was 14 years.

Mr. LAWRENCE ABEL (London), who said that cancer killed one person every six minutes in this country, and cancer of the colon one person every fifty minutes, described certain points in diagnostic technique. In assessing the main symptoms of the disease he stressed the importance of rapidly developing anaemia and loss of weight. He suggested that their radiological colleagues should use very weak solutions of barium, because more could be learned from the result in that way. Air replacement after barium was also sometimes helpful. With regard to operation, he advised against blind caecostomy or colostomy and felt it important to emphasize even in that gathering that the object of surgical manœuvre was to ensure the removal of the widest possible area of lymphatic drainage, together with not only the tumour-bearing portion of the bowel but all the colon which was supplied by the vessels that had to be ligated. Removal of the extensive lymphatic field entailed ligation of the main arteries as closely as possible to their points of origin. Another point in technique was the placing of clamps on the bowel to prevent dissemination of cancer cells. The only solution which he believed effectually killed cancer cells in the lumen of the bowel was 1 in 500 perchloride of mercury. In spite of more radical operations and more frequent resections, thanks to modern anaesthesia and antibiotics and pre- and post-operative care the mortality rate had been halved. Propaganda directed to the public, and to their family-doctor colleagues, should ensure that these cases were referred early to a surgical team, and the results might then show still further improvement.

Mr. PHILIP R. ALLISON (Leeds) discussed cancer of the oesophagus. Negative *x*-ray examination of the oesophagus should not be taken as final evidence of the absence of carcinoma. Any patient with dysphagia, even if only for a day or two and passing off, should be investigated; it was no use waiting until the dysphagia recurred. Bronchoscopy should always be done, because the tendency of these conditions to spread was considerable. He praised Souttar's tube, which he regarded as a wonderful apparatus.

The topic was further discussed by Dr. R. H. SWEET (Boston); and cancer of the stomach was the subject of papers by Dr. S. F. MARSHALL (Boston) and Professor DIGBY CHAMBERLAIN (Leeds), and cancer of the skin by Sir ARCHIBALD MCINDOE (London) and Dr. W. G. HAMM (Atlanta).

Cardiovascular Disease

In a concurrent session the subject of cardiovascular surgery was taken. Dr. MICHAEL E. DEBAKEY discussed the surgical treatment of aneurysms of the aorta by resection; Mr. C. G. ROB, the reconstruction of the large arteries; Mr. R. C. BROCK, modern techniques in intracardiac surgery; Dr. F. L. GERBODE and Mr. DICKSON WRIGHT, cardiac arrest; and Mr. A. MICHAEL BOYD, the diagnosis and treatment of obliterative arteritis of the lower extremities.

Sir JAMES LEARMONTH discussed the principles of treatment of arteriovenous fistula. These principles were, he said, the preservation or restoration of adequate blood volume, maintenance of adequate blood pressure, preservation or restoration of normal haemoglobin, and restoration to normal of the diseased or injured tissue.

The session concluded with a film, preceded by a few words by Dr. ALFRED BLALOCK (Baltimore), illustrating the creation in a young child of an artificial ductus in the treatment of the tetralogy of Fallot. The film was first shown at the clinical congress of the American College of Surgeons last year.

Recent Advances in Surgical Procedures

On the last day of the meeting, May 19, many papers were presented on surgical procedures. Sir CLEMENT PRICE THOMAS (London) gave a review of the surgical treatment of pulmonary tuberculosis. He had had experience of 220 cases submitted to resection during the last five years. The deaths following operation had numbered 18 (13 early and 5 late). Both he and his partner in the discussion, Dr. J. C. JONES (Los Angeles), presented a mass of statistics. Dr. Jones spoke of 729 cases of major operation and 542 of minor, carried out in the period 1943–54, during which the proportion of major operations had steadily increased. The mortality after resection for pulmonary tuberculosis had been 8% in males and 5.4% in females, and 75% of the patients were still active and working.

Adrenalectomy in Advanced Cancer

Sir STANFORD CADE (London) discussed recent advances in surgery of the adrenals in advanced cancer, and presented what he called a modest series of adrenalectomies. This comprised some 40 patients on whom he had carried out the bilateral operation. It was dangerous, he said, to draw conclusions on the effect of any therapeutic procedure from so small a series, and even more dangerous to do so after a period of only eighteen months; yet he thought this method could be studied even in a small series, and he gave particulars of four cases of patients who had previously undergone the orthodox methods of treatment—surgical, radiotherapeutic, hormonal—and in all of whom the disease was widely disseminated. They had all failed to respond to other methods, and there seemed to be every justification for resorting to adrenalectomy. It could never be said in advance that bilateral adrenalectomy would be successful. He had not been able to find any relationship between the histological structure of the tumour and its response to the operation. If adrenalectomy was going to be a failure it would be an immediate and complete failure, and if successful it would be successful immediately, though not completely. His operative mortality among 40 patients, some of them in the last stages of disease, was 15%. In nine cases excellent results had been obtained. He considered that bilateral adrenalectomy in the control of cancer was well worth doing.

Professor J. GARROTT ALLEN (Chicago) discussed surgical treatment in Cushing's syndrome. The considerable surgical risks involved in attacking basophilic adenoma of the pituitary had encouraged a tendency to do bilateral adrenalectomy, which, however, failed to get at the primary

problem. He mentioned the value of cortisone during the pre-operative period and of cortisone plus A.C.T.H. for a brief time post-operatively.

Malignant Disease of the Hip-joint

Sir GORDON GORDON-TAYLOR (London) described the treatment of primary malignant tumours in the neighbourhood of the hip-joint (hindquarter amputation). His first operation of this kind was performed in 1922, and his latest was done on his 76th birthday a few weeks previously. At his hospital the operation had been performed 77 times. The operative mortality was some 14%, but several of the patients were in an almost hopeless condition. Of the 33 patients alive to-day, 30% had survived operation five years or more. The most favourable type of tumour from the operational point of view was chondrosarcoma; 25 operations for this type of tumour were done, and 75% of the patients were alive. He described the case of a woman who had a large tumour attached to the gluteus maximus region of the great trochanter and who was on the point of being sent to a home for the dying. He was reluctantly persuaded to operate. Sir years later this woman was alive and well. Disappointments were of course to be expected, but postponement of the decision to operate only worsened the outlook, and in some cases the results exceeded the most sanguine expectations.

Professor BRADLEY COLEY (New York) discussed the general subject of malignant disease in the neighbourhood of the hip-joint. Professor R. H. SWEET (Boston) and Mr. A. L. D'ABREU (Birmingham) gave their experiences of surgical treatment of achalasia of the oesophagus; Dr. R. S. DINSMORE (Cleveland) spoke on the changing status of hyperthyroidism; and Dr. W. E. ADAMS (Chicago) brought the session to an end with a film showing pneumonectomy for carcinoma.

Massive Gastro-intestinal Haemorrhage

At a luncheon discussion presided over by Dr. FRANK GLENN (New York) massive gastro-intestinal tract haemorrhage was presented from different aspects. Professor W. WALTERS (Rochester, Minn.) said that massive haemorrhage was almost always due to the perforation or rupture of a large blood vessel, but he had seen it occur as a result of multiple small erosions of the gastric mucosa, so small that they could not be seen gastroscopically or demonstrated surgically, but were visible only under the microscope. Mr. NORMAN TANNER (London) spoke on massive haemorrhage from the oesophagus. The oesophagus, he said, was not a frequent site of massive bleeding. Bleeding was sometimes seen as a symptom of oesophagitis, but only rarely was it massive. Massive bleeding had been associated with oesophageal paralysis. In many cases bleeding was due to portal hypertension. The mortality of this condition was heavy, and a number of survivors died of recurrent bleeding within a year or two. He had seen no cases where gastroscopy precipitated bleeding. Bleeding from oesophageal varices was a matter for medical management at first. If bleeding recurred twice, and after a minimum of 48 hours, then surgical intervention was indicated.

Mr. C. G. W. ILLINGWORTH (Glasgow) spoke on massive bleeding from the stomach. Bleeding sometimes occurred without relation to gastric ulcer, presenting a minute pinhead bleeding-point which could be seen only with difficulty. Atrophy of the mucous membrane was a factor, and in a few cases carcinoma or indeed multiple carcinomas might be implicated. Finally Mr. IVOR LEWIS (Rhyl) dealt with massive haemorrhage from the duodenum. An acute ulcer, he said, could burrow right through the intestinal wall and similarly could open up one of the large vessels. Of 196 cases of massive gastro-intestinal haemorrhage on which he had operated personally, only 30 were due to duodenal ulcers.

Hand Surgery

The final session of the conference was occupied with a panel discussion on hand surgery. Professor MICHAEL MASON (Chicago) acted as moderator, and the collaborators were Mr. PATRICK CLARKSON (London), Dr. G. E. CLOUTIER (Montreal), Mr. R. G. PULVERTAFT (Derby), and Mr. WILLIAM GISSANE (Birmingham). Mr. Gissane said that conservative treatment in the right case gave ideal results, but all too frequently this treatment was surprisingly disappointing. Every case must be considered on its merits. It was utterly wrong to resort to open methods only when closed methods had failed. By doing so, very often the opportunity was lost of getting functional repair. To get a good functional result required attention not only to the bone but to the soft tissues also.

During the day's proceedings Sir CECIL WAKELEY, P.R.C.S., gave a talk on the relationship of the Royal Family, from George III onwards, with the Royal College of Surgeons, and showed a motion picture illustrating the laying of the foundation stone of the new building by Queen Elizabeth II on May 5, 1953.

The thanks of the American visitors to their British hosts were voiced by Dr. PAUL HAWLEY, Director of the American College of Surgeons.

BRITISH ORTHOPAEDIC ASSOCIATION

ANNUAL MEETING AT BUXTON

The annual meeting of the British Orthopaedic Association was held at the Devonshire Royal Hospital, Buxton, on May 6–8, under the presidency of Professor BRYAN MCFARLAND.

Syme's Amputation

Mr. J. H. SHELSWELL (Stanmore) spoke about Syme's amputation, an operation with a much better reputation in Canada than in this country. He had reviewed the Syme's amputees from the material available at Roehampton; of 534 cases, the 302 patients operated on before 1939 were chosen for assessment, and a follow-up on 66 of these was done. Two-thirds had had no significant trouble. Twenty-three per cent., including immediate failures, needed re-amputation, and, as Mr. LEON GILLIS pointed out in the subsequent discussion, this was no higher than the proportion of failures after the standard below-knee amputation. Syme's amputation had no place in the neuropathic limb or in those with vascular failure, and it was seldom indicated in women, who had no means of concealing the necessarily bulky and obvious ankle-joint in the prosthesis. But for the working man it was a most satisfactory operation, enabling him to stand and walk for long hours and even to play games. It was particularly advantageous for the double amputee, and Mr. Shelswell concluded that a properly done Syme's amputation was an excellent and long-lasting operation.

Review of 650 Arthroplasties of the Hip

Mrs. M. M. SHEPHERD (Birmingham), in an excellent and painstaking review of 650 arthroplasties of the hip, described how these cases had been followed up for a maximum of six years from operation, which were nearly all of either the vitallium cup or acrylic head type. They were assessed according to pain, range of movement, the patient's evaluation, and the objective estimate of function. Out of the great mass of figures available certain facts emerged. Excepting loss of pain, stability and satisfactory unconscious control of the hip were of greatest value to the patient, but the better the range the better on the whole was the result. Even so the mobility index (Gade) was not much worse in the poor than in the excellent results. The presence of slight residual fixed flexion seemed to give improvement, but transplantation of the trochanter delayed a good result. With regard to durability, cup arthroplasties went on improving up to four years, when 45% had good or excellent results; after five years 54% had poor results. The Judet arthroplasty was characterized by quicker recovery, but the patients deteriorated sooner and progres-

sively. Not all arthroplasties, however, deteriorated in later years, some with no apparent peculiarity retaining their excellence unchanged for many years. Mrs. Shepherd believed that arthroplasties with no inserted foreign material lasted best, then those with unfixed inserts—for example, cups—and lastly those with fixed prostheses. The percentage of good results was higher in unilateral than bilateral cases, and in the latter was higher when only one hip was operated on. The massive amount of material embodied in this impressive paper fell beyond the scope of a brief report.

Mr. K. H. PRIDIE (Bristol) expressed his dissatisfaction with the Judet arthroplasty, which he maintained should be reserved for those with a brief expectation of life. In his hands 5–10% would fracture their prostheses. Even at a year marked flattening and wear of the head was to be seen, and he thought that lack of this flattened facet was evidence that the prosthesis was rotating in the femoral neck. In his survey, 20% had loose prostheses, though a period of plaster fixation might fix them again. As an alternative to replacing the head when fracture or a poor result necessitated further operation, he considered the Girdlestone "pseudarthrosis" procedure satisfactory.

Kyphoscoliosis

Mr. J. I. P. JAMES (London) called attention to the lack of British work on the subject of kyphoscoliosis, although there was an extensive German literature about it. Apart from the deformities (usually mild) occasionally seen in Pott's or Scheuermann's disease, he classified his 27 cases into (1) congenital; (2) those associated with otherwise typical idiopathic scoliosis; and (3) those seen with neurofibromatosis. In the first group radiographs or operation displayed the malformation, but even early films of the second group showed no vertebral abnormality. Most congenital cases occurred in the lumbodorsal region, but there was a small group in the cervico-dorsal region. The deformity was progressive and severe, and might cause paraplegia. Early operation was indicated, but fusion was difficult to achieve.

Mr. R. ROAF (Liverpool) reported an operation of wedge excision of the vertebrae for scoliosis. In the past there had been general fear of direct operation emanating from the difficulties encountered in attempting excision of hemivertebrae. With his experience of antero-lateral decompression, combined with skilled anaesthesia and plaster work of the highest order, he could say that he had found no great difficulty in doing what was really a lateral osteotomy of the spine, and he described the technique. It was stressed that this was not an easy operation for routine use, but was suggested tentatively for those curves not responsive to other methods.

Pros and Cons of Hip Arthroplasty

A debate was held on the motion: "In the opinion of this house all methods of arthroplasty of the hip have failed to achieve their purpose." In spite of spirited arguments from the openers and the considerable number who finally voted in agreement with the motion, few could be found to speak whole-heartedly in its favour, and the motion was lost by a substantial majority.

Mr. K. I. NISSEN (London), proposing the motion, based his attack on hip arthroplasty on four counts: (1) the serious post-operative complications that could occur; (2) early deterioration; (3) the expense of the seemingly endless physiotherapy required; and (4) the faulty conception of the operations due to ignorance of the true pathology. One concept of vascular degeneration in the femoral head had been exploded by recent work at Oxford. Any pain-relieving operation reduces the blood supply of the hyperaemic head, but the arthroplasties interfered with it too extensively. The more British operations of McMurray's displacement osteotomy, Girdlestone's pseudarthrosis, or arthrodesis could be relied on to give equivalent or better results, and the reason they were not in favour with younger surgeons, was that the latter had little experience of them, the result being permanently good and not necessitating the patient's return to the surgeon. In most arthroplasties of all types the head eventually disappeared to leave some form of pseudarthrosis.

Mr. W. A. LAW (London) opposed the motion. After saying that there was no universally applicable hip operation, he enumerated the essential requirements of a good arthroplasty: (1) a joint must be made; (2) the pain of the arthritic joint must be alleviated and that produced later from over-fatigue of the controlling muscles must be limited; (3) fixed deformity must be corrected; (4) the new joint must be stable; and (5) an adequate range of movement must be produced, though a stable joint with small range was greatly preferable to an over-free joint where muscle control was poor and fatigue-pain therefore marked. With these criteria he maintained that cup arthroplasty was a good operation, the beneficial results of which lasted better than Mrs. Shepherd's investigation suggested. Patients asked him to do an arthroplasty on their second degenerating hip 5–10 years after one had been done on the first hip. But he stressed that careful selection of patients was essential. Obesity was not a contraindication, but the surgeon must be satisfied that the patients had the morale to pursue the necessarily arduous aftercare, and Mr. Law mentioned private patients favourably in this connexion. They must be warned of and understand the limitations of the result to be expected. The essential exercises could perfectly well be done at home, but circumstances often made prolonged supervision in the physiotherapy department essential. He did not look on cases needing revision as "failures," which was suggested by Mr. Nissen to be their proper description, but considered revision as an essential part of the treatment of the rheumatoid hip.

Mr. N. CAPENER (Exeter) seconded the motion. He said that we had not yet overcome the difficulties of certain essential mechanical conditions: (1) the new joint surfaces must have not only congruity but conformity of hardness; (2) there must be proper lubrication; and (3) the problems of leverage and adequate power must be solved. Present methods were incompatible with the above requirements. He estimated the cost to the nation of an arthroplasty at £200, which he looked on as very expensive for an operation doomed to failure. According to Mrs. Shepherd's figures deterioration set in five years after a cup arthroplasty and two years after an acrylic head, which, on the basis of the life-expectancy charts of insurance companies, should confine the former operation to the over-80's and the latter to the over-90's.

Mr. LLOYD GRIFFITHS (Manchester) seconded for the opposition. He denied that the traditional British operations relieved pain, and compared their results with those obtainable by taking the local waters. Arthroplasty was in a state of rapid evolution, and even the best of operations, like aeroplanes, were liable to temporary "grounding." He considered even the present results as well worth while, and pointed out that little progress would be made if surgeons must always await exact pathological elucidation of the problem.

In the subsequent debate, Mr. R. G. TAYLOR (Oxford) said that good results could be obtained in a properly done Girdlestone's pseudarthrosis. Mr. W. E. TUCKER (London) thought it advisable to make patients write down their pre-operative complaints as objective evidence for comparison with their later troubles, and Mr. H. OSMOND-CLARKE (London) said that arthroplasty had no place in the young patient.

Professor MERLE D'AUBIGNÉ (Paris) said he thought that all the failures of arthroplasty were due to technical errors. It took perhaps 200 arthroplasties to learn the art. He reported a much lower failure rate than the British figures, and stressed the importance of providing the correct length of neck and of correcting anteversion. He thought the results on the whole did not deteriorate in later years; indeed, some cases classed as only "fair" a year after operation became "good" with further passage of time. Mr. K. H. PRIDIE (Bristol) supported the advantages of the

d'Aubigné type of prosthesis. Sir REGINALD WATSON-JONES (London), while maintaining that arthrodesis was incomparably the better operation in the young, said he would vote against the motion as it was worded. Mr. JOHN CHARNLEY (Manchester) spoke of the advantages, essentially of principle rather than technique, of his operation of central dislocation of the hip, and thought that arthrodesis was a good operation even in the elderly, particularly those of wiry build.

Dr. ROBERT JUDET (Paris) gave figures to illustrate the good results of acrylic-head arthroplasty and recommended the new prosthesis with an oblique base. He pointed out that the crushed cancellous bone around the stem of any prosthesis was in a state comparable to a bone graft, and that therefore weight-bearing should be delayed two months, until revascularization of the trabeculae was advanced. Acetabular changes resulted from incongruity of the prosthesis, which should be of exactly the right size. Fractures of the prosthesis were now seldom seen in France, owing to a better acrylic resin. Mr. J. H. MAYER (Tunbridge Wells) thought the poor results were due to failures on the part either of the surgeon or of the material, and advocated the use of metal prostheses rather than acrylic resin.

Acrylic Prostheses in Fractures of the Femoral Neck

On May 8 the meeting was under the chairmanship of the vice-president, Mr. A. CHANCE.

Mr. C. M. M. MURRAY (Portsmouth) presented a review by Mr. G. N. GOLDEN (Guildford), Mr. A. G. ORD (Portsmouth), and himself of 60 cases of fractured necks of femur treated by primary replacement with Judet's acrylic prosthesis. There was no immediate operative mortality, but seven died while still in hospital. Later complications included two dislocations, two fatal cases of infected haematoma, one broken prosthesis, late ossification in the capsule, and late varus deformity. At 18 months over 80% had a satisfactory result, and he recommended the operation for the older age group, especially those with high or vertical fractures.

Mr. J. C. F. CREGAN (Manchester) gave a review of 65 cases of high fracture of the femoral neck similarly treated. In contrast to satisfactory immediate results, by the third year 85% suffered increasing pain and disability, and by the fourth year results were even worse. He thought that the integrity or otherwise of the region of the calcar femoralis had an important bearing on these results.

Mr. K. H. PRIDIE (Bristol) pointed out that with a Smith-Petersen nail 50% of patients at five years had a hip indistinguishable from normal, and deplored the use of an acrylic head as immediate treatment, a view supported by Professor D'AUBIGNÉ. Dr. ROBERT JUDET confined his recommendation of the operation in this connexion to the very elderly.

In further discussions Professor MICHAEL MASON (Chicago) and Mr. R. G. PULVERTAFT (Derby) spoke about wounds and injuries of the hand; and Mr. H. R. LUNT (Derby) gave a demonstration of the results of treating tuberculosis of the hip by a method aiming at shorter hospitalization, a greater range of movement, less epiphysial dysplasia, and less shortening.

A rehabilitation workshop has been developed by British Railways (Western Region) at Swindon. It will provide productive work for convalescent patients and an occupation of therapeutic value by adapting machinery to give graduated work to a selected group of muscles or to increase movement in one or more joints. The medical officer visits the workshop daily and considers the work of the patients with the assistance of the workshop foreman. A time limit of eight weeks, with some exceptions, will be given to patients in the workshop. Admission is entirely voluntary. The men begin work ten minutes later and finish work ten minutes earlier than the normal factory hours to enable them to avoid the usual rush in the approaches to the works. The number at present employed is ten.

Reports of Societies

MASS MINIATURE RADIOGRAPHY

Who Should be Examined?

A joint meeting of the North-western and Midland Tuberculosis Societies took place at the Cheshire Joint Sanatorium, Market Drayton, on May 8. The chairman was Dr. T. W. LLOYD. In a discussion on "What is the place, if any, of mass radiography?" the opening speaker was Dr. E. SNELL, who believed that mass radiography had indeed a place in the early diagnosis of pulmonary tuberculosis and other chest diseases, and that the only reasonable argument against its use was that of financial stringency. Mass radiography units could be used in four ways: (1) as a mobile unit visiting factories, etc., in a district and *x*-raying all employees; (2) as a mobile unit visiting specially selected factories and industries which are known to carry a heavy hazard of tuberculosis; (3) as a static independent unit concentrating on selected cases—for example, referred by general practitioners, men called up for National Service, etc.; (4) as a static unit situated in and operated by the chest clinic, also concentrating on selected cases—for example, from general practitioners, school medical officers, antenatal clinics, contacts, etc. Dr. Snell produced figures to show that the yield of tuberculous cases was much greater in selected groups. In 1953 nearly one-third of the new cases of tuberculosis in Liverpool were picked up by mass radiography. Apart from the number of cases found, they are discovered earlier, when they are more amenable to treatment. In Dr. Snell's opinion mass miniature radiography units should be operated from chest clinics and should devote their time to selected groups.

Pros and Cons

The next speaker, Dr. GEORGE LUNTZ, in an opening summary of the extent of mass miniature radiography in this country, said that up to the end of 1952 over 10½ million examinations had been done by 63 units, and that in 1952 18% of all cases of respiratory tuberculosis had been discovered by mass miniature radiography. In view of the fact that the present number of units allowed less than 10% of the population to be examined yearly it was important to consider whether any group of the population should have priority, and whether any group should be re-examined. There were three main ways of applying mass radiography: (1) True mass miniature radiography—that is, surveys of whole populations, the aim being to *x*-ray every individual in the community. Such surveys had been undertaken in Stockholm (80%), and in the Rhondda Fach (89%). A similar survey was in progress in Salford. (2) Group radiography, where the units concentrate on selected groups which are likely to yield the most cases. (3) Individual radiography, where members of the public can attend a mobile or static unit, either on their own initiative or because they have been sent by their doctor.

The problem, Dr. Luntz continued, was to decide which was the best method, and whether in fact mass radiography had any place at all. When used indiscriminately it was an expensive way of finding cases (£10 to £600 per case), and, even so, less than 20% of cases of tuberculosis were found by this method. Another point against it was that a normal *x*-ray finding might lull the subject and his doctor into a false sense of security, and subsequent symptoms might be ignored. Ideally radiography should be repeated annually, but this was impossible. Dual observer readings were necessary to prevent lesions being missed. Although mass miniature radiography was originally designed for tuberculous case finding, it detected many non-tuberculous abnormalities in heart and lungs, and with the rising mortality due to bronchial carcinoma mass radiography on the vulnerable age groups might make a valuable contribution.

Dr. R. STALKER was convinced of the value of mass miniature radiography, but thought that there could be

improvements by reducing the amount of record keeping, thus freeing some of the clerical staff to assist the secretary in the canvassing of susceptible groups. He gave some figures from his own unit showing that the yield of new cases of tuberculosis fell from 4 per 1,000 in 1942 to 1.2 per 1,000 in 1953. He considered that in industry repeat protective surveys were of doubtful value, though they were justifiable in, for example, mental hospitals. Mass miniature radiography in schools where a case of active pulmonary tuberculosis had occurred was valuable, but it was doubtful whether routine surveys in schools were worth while. The 100% geographical survey was the ideal, but was impossible, and became increasingly difficult with the size of the town. It was agreed that there was a high proportion of tuberculosis in the non-attenders in a general population survey.

Larger Surveys

Dr. Stalker thought that mass miniature radiography should be kept mobile and should *x*-ray males or young females as individual members of the general public in preference to industrial workers. He described the Manchester Regional Hospital Board policy of "miniature" as well as "mass miniature" radiography, which was implemented by having 4 in. by 5 in. or 70 mm. units in major chest clinics for *x*-raying selected groups. He mentioned the Salford survey by six mass miniature radiography units working simultaneously on a population of 170,000: powerful though this was, it was small by American standards. He proposed that two or more regional boards in this country should combine for large surveys on the American plan, where they used 22 units for towns of over 100,000 and aimed to *x*-ray 80% of the population in four weeks. There was a case to be made for combining mass miniature radiography with B.C.G. injections in the 15 to 25 age groups.

The fourth speaker, Dr. L. A. MCDOWELL, said that the function of mass miniature radiography was to assist in the eradication of pulmonary tuberculosis, which it could do by finding the infective, and especially the chronic infective, cases of tuberculosis. These cases usually had symptoms, and should be sent from the doctors' surgeries to the mass miniature radiography units. General practitioners and industrial medical officers should be persuaded to send all patients with symptoms for radiological examination. This did not mean that the mass miniature radiography service was setting up as a rival to the chest clinic. It was saving the chest physician from seeing large numbers of cases, of whom 9/10 had normal radiological findings. It also saved money and time, and the patients preferred it. He suggested that mass miniature radiography units should be withdrawn from industrial surveys and should go on a regular circuit of large centres of population, where they could examine people with symptoms and other groups such as contacts, school leavers, National Service recruits, etc. By this means each unit should be able to do 40,000 to 50,000 examinations yearly and provide the chest physicians with 400 new cases per year.

In the discussion which followed Dr. J. R. SINTON pointed out that most of the speakers had been advocating "miniature" and not "mass miniature" radiography, and that this was best undertaken by the chest clinic. He was against the principle of *x*-ray before clinical examination. Dr. J. ASPIN thought that the mobile factory survey would have to continue because the public expected it. In his opinion static units should be an integral part of the chest clinic service. Dr. D. MORRISON SMITH said that in finding infective cases of tuberculosis it would be cheaper to examine sputa than *x*-ray patients.

Dr. W. GRIFFEL thought that mass miniature radiography found too many cases which could not be treated. Dr. COTTON CORNWALL thought that some cases which were discovered did not have clinical tuberculosis and should not be "labelled." The opening speakers replied to many of the points raised and agreed that it was soul-destroying to do only mass radiography: it should be combined with chest clinic work.

THE PROBLEMS OF POLIOMYELITIS

Are there localities in this country which poliomyelitis specially tends to visit, or in which it particularly cares to linger? This was the question that Professor BRADFORD HILL, F.R.S., set out to answer in the presidential address delivered to the Section of Epidemiology of the Royal Society of Medicine on May 21.

The most striking features of the geographical distribution of poliomyelitis during 1919–46, he said, were the unexpectedly low numbers of cases in most of the counties in Wales and Northern England, and the unexpectedly high numbers in three groups of contiguous counties—one in the north-east Midlands, another including Shropshire, Hereford, and Radnor, and the third in the south stretching from Devon to Kent and Essex. There was an appreciable similarity between this pattern and that found in the years of higher incidence after 1946. There were reasons for believing that these geographical differences were not the result of differences in the accuracy of diagnosis or thoroughness of notification.

A detailed study of epidemics in the large towns showed that only twenty experienced a substantial epidemic between 1919 and 1946, and only twelve had more than one epidemic. But these twelve included nine in which poliomyelitis was epidemic three or four times during the quarter of a century—namely, Bristol, Oxford, Sheffield, Plymouth, Kingston-upon-Hull, Cardiff, Portsmouth, Manchester, and Birmingham. Why certain towns should have been picked out for visitation was a mystery, but Professor Hill drew attention to the fact that half of the twenty towns were ports, and of the nine towns with repeated epidemic experiences six were ports. If the epidemics were the result of imported infection, it was of interest to note that they did not spread widely. Nevertheless a study of incidence in administrative counties showed, for instance, that the epidemic years in Lincolnshire (Lindsey) were also those of the epidemics in Hull (1927), in Grimsby (1930), and in both of these ports (1938), and a similar coincidence was found in the timing of epidemics in Plymouth and Cornwall and in Portsmouth and Hampshire. Two months before the famous Broadstairs epidemic in 1926 there had been small but sharp outbreaks at Sheerness and Queenborough in the mouth of the Thames. The lack of epidemics in certain large towns between 1919 and 1946 might be expected to have made them vulnerable to later infection. The fact that some of them remained little affected during the widespread infection of 1947 was therefore very striking.

Change in Age Incidence

It has been shown[1] that in the years 1944–8 a significantly higher proportion of reported cases of poliomyelitis were over the age of 5 years than in the years 1912–19. Professor Hill, by reference to the reports of medical officers of health of towns where epidemics occurred in the intervening years, had come to the conclusion that there was little sign of change in age incidence until 1938, when the country experienced the sharpest epidemic up to that time, and when the change in age incidence became quite marked. It persisted until 1947, and had since become even more marked. Using the same source of information, he concluded that there had been no change in the ratio of arm to leg paralysis as a result of the great increase in inoculations since 1942.

One of the purposes of epidemiology is to define problems needing special investigation, and Professor Hill has indicated several here. If, as appears from the figures, fresh introductions of infection frequently took place through the ports, why was spread so limited? If the shift in age incidence to older people was the result of their not being immunized when young owing to improving standards of hygiene, what is the explanation of the comparatively abrupt change in 1938? Why do certain cities have repeated outbreaks, while others with similar environmental conditions escape? And why does the disease tend to reappear in certain localities?

[1] Benjamin, B., and Gale, A. H., *Monthly Bull. Minist. Hlth (Lond.)*, 1949, **8**, 208.

Correspondence

Intravenous Ergometrine and the Undiagnosed Second Twin

SIR,—The value of intravenous ergometrine in the reduction of third-stage haemorrhage has been proved beyond doubt.[1] However, Drs. J. K. Russell, D. Tacchi, and Anne L. M. Graham (*Journal*, May 15, p. 1129) have drawn attention to the risk to an undiagnosed twin when intravenous ergometrine is given before the first child has been completely delivered. When ergometrine is given at the crowning of the baby's head or with the delivery of the shoulder, the rapid cessation of the placental circulation increases the risk of asphyxia neonatorum, especially by inhalation of mucus. This fear caused us, at Sorrento Maternity Hospital, to delay the injection until the baby has been born, when the uterus can be palpated abdominally before giving the ergometrine and all the risk of an undiagnosed twin avoided.

Out of 1,520 consecutive deliveries in this hospital, 130 cases were selected for intravenous ergometrine because they were considered liable to post-partum haemorrhage (grand multiparae, twin labour, inertia, previous post-partum haemorrhage, also after forceps and breech deliveries). In these cases 0.5 mg. ergometrine was given intravenously after the baby was born, and the loss of blood was no greater than that described by Drs. J. D. Martin and J. G. Dumoulin. In five cases where manual removal of the placenta became necessary, a slight contraction ring was found which relaxed readily when 3 min. (0.2 ml.) amyl nitrite was inhaled in addition to the general anaesthetic (nitrous oxide, oxygen, and ether). In no case was any difficulty encountered, although in all five cases part of the placenta was definitely adherent to the uterus. Surely this experience disproves the prevalent idea that it is necessary to administer ergometrine prior to the complete delivery of the baby when, in actual fact, there may be some danger?—I am, etc.,

Birmingham. JEAN L. HALLUM.

REFERENCE

[1] Martin, J. D., and Dumoulin, J. G. (1953). *British Medical Journal*, 1, 643.

SIR,—In their article Drs. J. K. Russell, D. Tacchi, and Anne L. M. Graham (*Journal*, May 15, p. 1129) state that they had been fortunate in that none of their undiagnosed twins had been lying transversely, in which event a difficult intrauterine manipulation might be necessary, with risk to mother as well as child; nor do they appear to have experienced trouble from spasm of the cervix after administration of the drug. The following case illustrates both these complications.

An unbooked patient, a gravida-2, aged 28, was admitted to Queen Charlotte's Hospital as an emergency case on March 15, 1954. She was one of twins, but her pregnancy had been uneventful apart from a threatened abortion at two months. Labour commenced spontaneously at 33 weeks and the contractions became strong and frequent. She had two injections of pethidine, 100 mg., but the cervix did not dilate, and she was accordingly admitted to hospital after 44 hours in labour. Her general condition then was good; the uterus was not relaxing between frequent contractions, and it was not possible to determine per abdomen the presentation or position of the foetus, as the uterus was so hard. The fundal height was normal for 33 weeks, and a foetal heart was heard beating regularly at 170 per minute, thereafter remaining between 150 and 128 per minute. Vaginally, the presentation was found to be vertex with the head in mid-cavity in the R.O.A. position. The cervix was fully dilated and the membranes had ruptured. The head advanced very slowly, and, after 1½ hours in the second stage, an easy forceps delivery was performed under cyclopropane, gallamine triethiodide, nitrous oxide, oxygen, and trichlorethylene. The cord encircled the neck once, and was very tightly applied. The head and neck above this level were intensely cyanosed and swollen. Although the heart was beating at birth, respiration was never established. The foetus weighed 3 lb. 8¼ oz. (1.58 kg.).

Intravenous ergometrine, 0.5 mg., was given with the birth of the anterior shoulder. The uterus contracted firmly, but seemed rather large, and vaginal examination revealed the bag of waters of the undiagnosed second twin protruding into the vagina. The membranes ruptured during examination. The cervix now admitted only two fingers and the presentation of twin 2 was a shoulder. Time was allowed for the cervix to relax and an inhalation of amyl nitrite, 5 minims (0.3 ml.), was given, with some effect. As soon as a hand could be passed through the cervix, a difficult internal version was performed. A foot was brought down, followed by the other, and a breech extraction was performed. The extended arms were flexed and brought down. There was delay of 10 minutes in delivery of the head by the Mauriceau–Smellie–Viet manœuvre, as the cervix was not completely dilated. A stillborn foetus weighing 3 lb. 8¼ oz. (1.58 kg.) was delivered 70 minutes after the first twin. The placenta failed to separate and had to be removed manually. The uterus felt normal. The total blood loss was 14 oz. (0.4 l.) and the patient's condition was good throughout. She remained apyrexial and demanded to return home by ambulance on the third day of the puerperium.

Post-mortem Examination (Dr. Claireaux).—Twin 1: Intense engorgement and severe subcutaneous oedema of the head and neck above the level of the cricoid cartilage, the colour of the oesophagus changing abruptly at this level. Subpleural and thymic petechial haemorrhages. Subarachnoid and intraventricular haemorrhages. Twin 2: Subpleural and subepicardial haemorrhages. No intracranial lesion.

I am grateful to Miss K. M. Robinson for permission to record this case.—I am, etc.,

London, W.6. ELLIS JONES.

Prolonged Cortisone Administration for Rheumatoid Arthritis

SIR,—The interesting article by Dr. W. S. C. Copeman and his colleagues on the management of rheumatoid arthritis with prolonged cortisone administration (*Journal*, May 15, p. 1109) once again raises the question not only of the criteria used for the evaluation of therapy, but also of our aims in treating this potentially crippling disease. In this well-observed and carefully followed up series of cases the authors, in their assessment, have correctly distinguished between the effects of therapy on functional capacity, joint involvement, and clinical and laboratory evidence of disease activity. The results were assessed largely on a practical functional basis, and the value of therapy appeared to rest chiefly on a definite functional improvement in 17 out of the 20 cases treated.

In spite of this, however, a number of cases showed radiological progression of damaged joints. In other words, although the treatment has been shown to be of practical value from the functional aspect, the disease has actually progressed from the point of view of joint damage. This may be the result of the natural course of the disease, but one cannot help but feel that increased use of damaged joints may be an important contributory factor. We may therefore ask ourselves whether, in treating rheumatoid disease over a prolonged period with a drug known to be non-curative, we should suppress symptoms and signs in order to encourage functional capacity. We may be justified in doing this with a short course of treatment in order to assist rehabilitation. On the other hand, in long-term treatment, encouragement of functional capacity may carry a danger of producing further joint damage. This applies particularly to the younger age group, where there is a greater opportunity for wear and tear of the joints over a period of many years. In such cases, our efforts should be directed chiefly to reducing rheumatoid activity. It is well known that the disease may undergo natural remission, and such remission is the best possible improvement short of a cure.

Having assessed and followed up many hundreds of patients treated with a variety of therapeutic agents, it is felt that, in rheumatoid disease, more emphasis should be laid on activity of the process than on functional capacity as a criterion in assessment. Although improved function

should be taken into account, reduction of rheumatoid activity must represent the major criterion for the effectiveness of any therapeutic agent.—I am, etc.,

Bath. L. MANDEL.

Pleural Effusion in Young People

SIR,—The recent Ministry of Health memorandum on prevention of tuberculosis[1] (see *Supplement*, April 17, p. 174) urges an intensification of the war on this disease on many fronts simultaneously. To the various measures suggested we would make a plea for the proper assessment and treatment of cases of pleural effusion in young people, amongst whom it is a common condition. On the basis of recent work in England[2] and some Scandinavian investigations[3 4 5] it can be calculated that, with the present rate of tuberculous infection in this country, at least 100 cases of pleural effusion will arise each year in schoolchildren alone per million total population. Most of these cases present with severe symptoms and are readily diagnosable. Indeed, the great majority are diagnosed, but the high probability of a tuberculous aetiology does not always seem to be sufficiently regarded. Many youngsters with pleural effusion receive no more treatment than a few weeks in bed followed by a few weeks more at a convalescent home. Too often the diagnosis of tuberculosis is not made because the doctor does not wish to cause anxiety to the parents.

Pleural effusion is a serious condition, being frequently followed by frank pulmonary tuberculosis. In our series[2] no fewer than 15% of girls who had what seemed to be a simple tuberculous pleural effusion between the ages of 10 and 16 developed obvious pulmonary tuberculosis during a follow-up period of six years. In young adults Thompson[6] reports an even higher incidence. In addition, Sibley[7] has shown that cases of pleural effusion run an appreciable risk of developing extra-pulmonary tuberculosis. These complications and sequelae are scattered over many years, and the short observation period often given to these cases is probably one reason why pleural effusion is too frequently said to be "benign." The seriousness of pleural effusion may be due, in a proportion of cases, to an underlying miliary tuberculosis which, for one reason or another, is not radiologically visible.

There seems good reason to advocate that pleural effusion in tuberculin-positive children and adolescents, in the absence of some definite alternative diagnosis, should be considered as tuberculous and should be thoroughly investigated and treated in special units where, of course, education can be continued. It appears likely that antibiotic therapy in selected cases, together with an adequate period of graduated rest and subsequent rehabilitation, will prevent the development of serious tuberculous trouble in many instances later in life, and will in consequence make a further contribution to the fight against this scourge, which, though retreating, still exacts too great a toll.—We are, etc.,

F. J. BENTLEY.
S. GRZYBOWSKI.

Brentwood, Essex.

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2 Bentley, F. J., *et al.* (1954). *Tuberculosis in Childhood and Adolescence*. N.A.P.T.
3 Nissen Meyer, S. (1949). *Statistical Investigations of the Relationship of Tuberculous Morbidity and Mortality to Infection*. E. Munksgaard, Copenhagen.
4 Gedde-Dahl, T (1948). *Tuberculoseinfeksjonen i lys av Tuberkulinmatrikkelen*. J. Grundt Tanum, Oslo.
5 Holmdahl, K. (1950). *Acta tuberc. scand.*, Supplement 22.
6 *Amer. Rev. Tuberc.*, 1946, 54, 349.
7 Ibid., 1950, 62, 314.

Psychiatry and General Medicine

SIR,—Perhaps it is unwise for one section of the profession to be over-critical of another. Most of us, after all, live in glass houses. Also, when Dr. Cyril Josephs (*Journal*, May 8, p. 1096) takes such pleasure in scoring off the psychiatrist, one wonders what is his unconscious motivation. Dr. Josephs is more than critical of psychiatric treatment and insists that psychiatry as a discipline must be measured by its success in curing patients. I do not think this is altogether a logical argument, and heaven knows where it would leave, for example, brain surgery, dermatology, and much of general practice. It is true that advances in treatment are nowhere more necessary than in psychiatry. Illnesses like schizophrenia fill thousands of hospital beds, and neurotics are said to throng practitioners' waiting-rooms. Are we then to give up the practice of mental health until a benevolent Government opens its coffers to research and hastens the psychiatric millennium?

I suppose no one is more conscious of the limitations of therapy, both physical and psychotherapeutic, than the mental hospital psychiatrist administering it. After all, far from burying his failures, he often has to live among them. E.C.T. and insulin are useful therapies and can transform abject misery into optimistic well-being. Certainly they are empirical and sometimes fail. I venture to suggest that this is also true of much in general medicine, despite recent advances. Psychiatry, of course, has other weapons, and the doctor's use of them depends on his opinions, his qualities of personality, and his psychotherapeutic skill. Here again, however, he can expend his resources without success, and therefore he tries to apportion his time wisely. The chronic neurotic, pitiful though his situation may be, is not only a poor prospect for intensive treatment but also uneconomical. There are so many others for whom the psychiatrist can do more.

Admittedly psychiatry has overplayed its hand. Too many films and stories have moulded the psychiatrist into the likeness of God and given him powers he sometimes forgets he does not possess. Dr. Hunter Gillies[1] put it well when he said: ". . . The myriad patients against whom the dice were loaded from the moment of their conception rarely figure in such selected material, and then only in the productions of our heavier and gloomier writers. But it is these patients who daily confront us, and our support of these handicapped people, valuable and indeed indispensable as it is, appears pedestrian beside the miracles that the public have been led to applaud."

Perhaps Dr. Josephs will consider these few points and arrive at a more balanced and charitable conception of our specialty. There is needed on the part of the general public a more enlightened attitude towards psychiatry and mental hospitals, and this will come more speedily if doctors show it first.—I am, etc.,

Aberdeen. J. K. W. MORRICE.

REFERENCE

1 *J. ment. Sci.*, 1953, 99, 321.

Anthrax Protective Antigen

SIR,—In your annotation (*Journal*, May 8, p. 1083) on anthrax protective antigen, you state: "The Pasteurian method of producing active immunity against anthrax . . . has hitherto not been superseded in the 70 years since it was introduced." This is not quite accurate. Sterne[1] and Stamatin[2] independently isolated an avirulent spore vaccine in 1937 which, although used in a living state, differs from the old Pasteurian vaccine in an important way. Whereas the Pasteurian vaccines contain organisms that are potentially virulent, the Sterne vaccine lacks an essential factor for virulence—namely, the polyglutamic acid capsule. This makes it perfectly safe to use and avoids the failures and disasters that occasionally occurred with the Pasteurian vaccines, and is a very important advance on these older vaccines. It has in fact been used on a very wide scale, particularly in South Africa, where several million head of cattle have been immunized without a single accident. By its use, anthrax among cattle has been virtually wiped out in that country. This is the strain that the Porton workers used for the production of their soluble antigen and called by them "Weybridge." With more justice to its discoverer, who sent it to the Ministry of Agriculture's laboratories at Weybridge, it should be named the "Sterne" strain.

It has been clearly shown that these living vaccines immunize by a local proliferation at the site of injection, liberating soluble antigen *in vivo* in the same way that it is liberated by virulent organisms in anthrax infection; but,

whereas lesions of the latter are progressive, the local lesion of the former is invariably retrogressive. The production of the soluble antigen on a large scale *in vitro* is obviously an important advance, and the Porton workers are to be congratulated.—I am, etc.,

Oxford. G. P. GLADSTONE.

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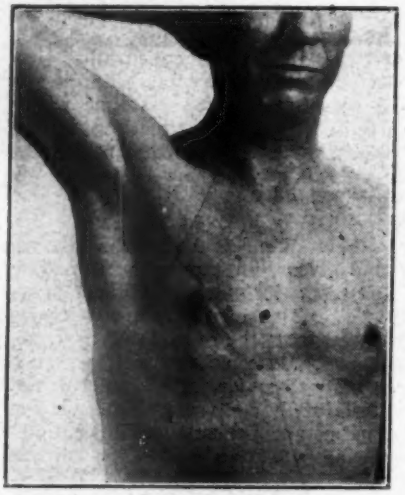
[1] *Onderstepoort J. vet. Sci.*, 1937, 9, 49.
[2] *C.R. Soc. Biol. (Paris)*, 1937, 125, 90.

Mondor's Disease

SIR,—We read with interest Mr. G. M. Lunn and Mr. J. M. Potter's article on Mondor's disease (*Journal*, May 8, p. 1074). At that time we had a patient with this condition of one month's duration. Although less evident than when first seen, the lesion is still well shown in the photograph.



The patient, a married male aged 57, attended in April, 1954. His general health was excellent, with no recent illness apart from osteoarthritis of both first metatarso - phalangeal joints. He had marked congenital clubbing of the fingers, and so had his son, while this was less prominent in his daughter and absent in his wife. A non-tender subcutaneous cord-like structure was palpable from the right anterior axillary fold to the level of the fourth right intercostal interspace. Just above the right breast it bifurcated, the less prominent of the two limbs of the bifurcation passing across the areola. The lesion was brought into prominence by abduction and external rotation of the arm and then caused marked puckering of the skin. There was no discoloration, but the patient stated that it was "a pinkish colour" on the third day after he first noticed it, but that it was normal the following day. The breasts were normal, no glandular enlargement was noted, and many pigmented moles were present on the chest and abdomen. The disease did not affect the patient's general health. There was no history of trauma, but three weeks before the lesion appeared the patient changed all the wheels of his car and noticed definite strain in the forcible jerking movements to loosen the bolts.

Unfortunately, the patient was unwilling to have a biopsy taken. We have only seen one other example of this condition.—We are, etc.,

London, E.4. E. A. W. MARIEN.
F. SANDERS.

Drinking Sea-water

SIR,—Air Commodore T. C. Macdonald's attempt (*Journal*, May 1, p. 1035) to discredit Dr. Alain Bombard's achievement in crossing the Atlantic in a rubber raft surely deserves some comment. He says dogmatically sea-water should not be drunk, and that Bombard's evidence for doing so is unsatisfactory. It is generally accepted that salt intake is necessary to replace that lost in the perspiration, which in a castaway may be excessive. The men in the Kon Tiki recognized this and took salt tablets with them; rather unnecessary, surely, when they were surrounded by salt. Then by accident they discovered that sea-water tasted very well in their gruel, and they continued to add it after this purposely. They also found that they felt better and their thirst was quenched more by adding between 20% and 40% of sea-water to their fresh water. For Air Commodore Macdonald to ignore this aspect of salt replacement by a certain amount of sea-water and advise castaways to wait for rain water, as in Bombard's case, for 21 days, is remarkable, surely, and seems to require some explanation and qualification.—I am, etc.,

Belfast. R. A. MCILRATH.

Anaemia

SIR,—May I make a few comments on Dr. R. O. Gillhespy's letter (*Journal*, April 24, p. 983) on the "Treatment of Pernicious Anaemia"? I would like to suggest that the case which he describes was not in fact suffering from Addisonian pernicious anaemia, but from a megaloblastic anaemia due to folic acid deficiency. Two factors should rule out a diagnosis of Addisonian pernicious anaemia, the first being that she had no absolute achlorhydria, and the second that she did not respond to vitamin B_{12}. As she responded to proteolysed liver she must have a folic acid deficiency—due either to malnutrition or to malabsorption, the second being much more likely, and a fat analysis of her stools might be helpful.—I am, etc.,

Edinburgh, 10. R. P. GOULDEN.

Racial and Religious Tolerance

SIR,—Dr. C. P. Seager is certainly right in deploring racial and religious intolerance (*Journal*, May 15, p. 1156). As a matter of principle we should always be aware of the difference between reasonable and prejudiced conducts wherever we meet them. Our colleague seems, however, to ignore the psychodynamic function of various prejudiced sentiments. Compliance, to a certain extent, with such tendencies serves a role similar to the avoidance of phobic situations or the performance of compulsive actions by a large group of patients. Therefore, as long as not much immediate harm to others results, prejudices of some sorts have to be put up with, because of a corresponding need for them in the prejudiced subject.

Indubitably, some professional men will find co-operation easier with colleagues with whom they feel at ease, and this fact must be considered however irrational the prerequisites of such mental ease may be. The same applies to patients whose anticipatory confidence in a doctor may be much disturbed if they have to suppress their prevailing religious or racial prejudices towards him. May Dr. Seager and other readers be referred to a book *Co-operation, Tolerance and Prejudice*?[1] It is heavy going and not well written, but explains in detail the phenomena in question.

We may be glad ourselves not to be dominated by unfriendly prejudices of the kind Dr. Seager has in mind, just as we should not like to have to comply with phobias or compulsions. But I cannot imagine the life of certain personalities without such "unreasonable" attitudes impelling them to select and avoid groups of fellow-beings in their daily social contacts. Only some of these sentiments are based on ignorance and automatic acceptance, and therefore capable of being discarded. The main thing is that prejudice, and intolerance based on it, should never be rewarded by approval or power; but we must wisely tolerate much of such manifestations.—I am, etc.,

London, N.W.4. S. LOWY.

REFERENCE

[1] Lowy, S., *Co-operation, Tolerance and Prejudice*, 1948. Routledge and Kegan Paul.

SIR,—When Dr. C. P. Seager (*Journal*, May 15, p. 1156) is a little older he may appreciate that the likes and dislikes of our colleagues and patients are to some extent to be respected. We choose our wives, our husbands, our food and drink, our friends, and our politicians as we will. This is freedom. We behave with courtesy to those persons we dislike, and allow them the freedom we ourselves enjoy. This is civilization. If the patient prefers a papist, a Jew, a negro, or even an Englishman or Scotsman, to anyone else, why should not his doctor? Likes and dislikes do not necessarily arise from faulty reasoning or "emotionally toned prejudice."—I am, etc.,

Cricklade. T. R. THOMSON.

Intravenous Iron

SIR,—I enjoyed reading the letter on intravenous iron by Drs. Frank Fletcher and E. London (*Journal*, April 24, p. 984). I am glad to see them admit that lethal factors in animals are not always related to factors producing reactions in man. I still cannot see, however, how increase of reticulo-endothelial activity *per se* can be invoked as the ultimate cause of reactions in man. Such abnormal activity is common in infections and reticuloses, yet no one invokes this as the ultimate cause of either. How can this evidence be marshalled? One method is surely to determine the presence of enlargement of liver, spleen, and lymph glands. These signs are commonly seen in the diseases mentioned, and also occur in serum allergy. It is strange, therefore, that no one has, to my knowledge, reported them so far to occur after injection of iron.

Their statement that reactions which follow the first administration of a dose of iron preclude an antigen–antibody response cannot go unchallenged. It is well known that severe anaphylactic reactions can occur in patients who have never had contact with the allergen before. I recall a patient of mine aged 16 years with no personal or familial allergic history who nearly died from anaphylactic shock following 100,000 units of intramuscular antidiphtheric serum given for the first time. In the *Lancet* (April 24, p. 873) a case is reported in which a girl died following a small test injection of antitetanus serum. This is the so-called "phenomenon of natural supersensitivity." Some argue that such cases do not exist, in that unknown contact with a previously sensitizing substance always occurs. This may well happen if the *complete* antigen has not been introduced—that is, as I mentioned in a previous letter (*Journal*, March 6, p. 583) hapten activity occurs.

Finally, I do feel that, although instability of the preparation used may be operating, yet the main factor in the rapid onset of such reactions is that of direct introduction of the substance into the blood stream, whether this be intravenous or intramuscular. This was one of the disadvantages stressed by protagonists of the administration of vaccine by mouth—for example, for treating dysentery.—I am, etc.,

Romford, Essex. I. M. LIBRACH.

Nutrition and Experimental Malaria

SIR,—The recent renewal of interest in the effects of nutrition of the host on the development of malaria parasites makes it seem appropriate at this time to recall some of the earlier work and to emphasize the importance of the caution expressed in an annotation which appeared about a year ago in the *British Medical Journal*[1]: "It does not necessarily follow that a substance is metabolized by parasites because it facilitates their growth when administered to the animal harbouring the parasites. . . ."

Passmore and Somerville[2] in 1940 published the first report of experimental work on the influence of nutrition on a malarial infection. They found no effect of a diet deficient in vitamins A and C on the course of infection with either *Plasmodium cynomolgi* or *P. knowlesi* in monkeys. Three years later[3] it was found that biotin deficiency specifically decreased the resistance of chickens and ducks to certain avian malaria parasites. The same year it was reported[4] that pantothenic acid favoured the survival and development of one of these avian parasites, *P. lophurae*, when it was maintained *in vitro* in suspensions of erythrocytes. These two findings set a pattern which subsequent experiments have fully supported: growth factors, depending on their nature (and, as later work showed, on their concentration) can either favour or retard the development of a malarial infection. The results with pantothenic acid led to the successful experimental use of analogues of the vitamin as antimalarial agents[5] and to the demonstration of the inability of *P. gallinaceum* to develop in chickens deficient in pantothenate.[6] Much additional significant information has since accumulated. Deficiencies in the host's diet of folic acid,[7] protein,[8] or nicotinic acid,[9] like biotin deficiency, favoured the development of avian malaria parasites, whereas a deficiency in riboflavin retarded the development of avian parasites,[10] and deficiencies in vitamin C,[11] methionine,[12] or para-aminobenzoic acid[13] retarded the development of simian malaria parasites. The effects of a milk diet on certain mammalian malaria parasites,[14 15] and their explanation in terms of para-aminobenzoic acid deficiency,[16] are well known to readers of the *British Medical Journal*. Despite all these facts, it would be premature to draw any conclusions concerning the nutritional requirements of malaria parasites. We must remember that the experiments referred to above relate to parasites growing in erythrocytes within a host animal, or at best to parasites growing in erythrocytes maintained for a short period *in vitro*. Recent work with *P. lophurae* has shown that when this organism is maintained extracellularly *in vitro* it requires coenzyme A[17] and not the pantothenic acid moiety of coenzyme A. It is likely that some of the other factors in the diet of the host which favour the development of the parasite do so only indirectly. They must be present in the diet of the host in order to permit the host to elaborate other substances which are the materials actually utilized by the parasite.—I am, etc.,

New York. WILLIAM TRAGER.

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Important Anomaly of Long Saphenous Vein

SIR,—In your medical memoranda of April 17 (p. 918) you had an admirable account of "An Important Anomaly of the Long Saphenous Vein" by Dr. A. J. M. Cathro. I would welcome an opportunity to stress this abnormality. Trendelenburg's operation for varicose veins is common, and in the course of the last three years I have, unfortunately, treated three cases of amputation, two above the knee and one below the knee, for the erroneous ligature of the femoral artery. In each case it was difficult to ascertain why this had occurred, but undoubtedly the femoral artery had been ligated, and this was probably due to the fact that it was not recognized that the long saphenous vein may pass spirally round the lateral side of the femoral artery. In these days of litigation it would seem most important for surgeons to be aware of the existence of this anomaly.—I am, etc.,

London, S.W.15. LEON GILLIS.

Infectious Mononucleosis

SIR,—Dr. S. Varadi (*Journal*, May 15, p. 1155), writing on infectious mononucleosis, states that whether one adopts the theory of one causal virus or of different closely related ones, the blood count is the most important test of infection and is most likely to reveal the diagnosis at an early stage: also that this diagnosis is not excluded by a negative Paul–Bunnell test. In my experience the blood count and the blood picture in cases of measles, mumps, and lymphocytic choriomeningitis may be indistinguishable from that of an infectious mononucleosis, which gives a positive Paul–Bunnell test. I have in the past seen an experienced haematologist report the presence of numerous Downey Type II cells in the blood of a patient whose Paul–Bunnell test was negative, and who subsequently developed a rising complement-fixation titre for lymphocytic choriomeningitis.

Should pathologists admit that the blood picture in the diseases mentioned above is indistinguishable from that of infectious mononucleosis, it is doubtful whether infectious mononucleosis with a negative Paul–Bunnell test can be regarded as a disease entity. I think it is closer to the truth to state that known and perhaps unknown diseases may have a blood picture identical with that of infectious mononucleosis. Therefore a disease giving this blood picture combined with a positive Paul–Bunnell test with the complete adsorption procedures could be called infectious mononucleosis. If the Paul–Bunnell test is negative, complement fixation tests for known virus diseases might give the diagnosis. If these tests are not done, or are negative, let us be honest and say the disease has not been diagnosed. As yet, I have not seen a positive complete Paul–Bunnell test in a case of measles, mumps, lymphocytic choriomeningitis, or other undiagnosed form of benign meningitis, although the blood picture in some of these cases was indistinguishable from that described by Downey for infectious mononucleosis.

London, N.12. PETER WOLF.

Women in Medicine

SIR,—Your annotation (*Journal*, May 15, p. 1143) draws attention to the dual responsibility of married women in medicine. This difficulty is now enhanced for those who have been overtaken by the new regulation requiring a pre-registration year of internship. The compulsory living-in during this year raises serious problems in the home, particularly for those who have young families. Would it not be feasible to permit living-out, provided that duties were not interfered with, at least for those women who took up medicine and incurred family responsibilities before this regulation was announced?—I am, etc.,

London, N.W.3. RUTH D'ARCY HART.

Renal Clearance of Creatinine and Urea

SIR,—In his article Dr. R. A. Kenney (*Journal*, May 15, p. 1130) has shown that in nine out of ten West Africans the (maximum) urea clearance was lower than the average normal value accepted in Great Britain and the United States (75 ml./min.): in eight of the ten, the value was less than 3/5 of the average normal. He has shown that the creatinine clearance is similar in West Africans and in Europeans, and states that other investigations not yet published have shown the identity of the glomerular filtration rate and the renal plasma flow rate in the two groups. From these results Dr. Kenney argues that the mechanism of excretion of urea in West Africans differs from that in Europeans. Such a conclusion is not justified by the evidence in his paper.

The table of urea clearances given by Dr. Kenney is meaningless, because we are not told how the six results from each subject are combined to give the values tabulated. If, as one suspects, the results were arbitrarily separated into those corresponding to urine flows over 2 ml./min. and those corresponding to urine flows under 2 ml./min., the grand means for all the West African subjects are differently weighted by individual results and no conclusions are possible. In any case no comparison is possible with the European subjects, because the number of these is not stated.

Dr. Kenney states that the African subject "fails to show the 'augmentation' phenomenon which is characteristic of urea excretion in the European subject." The "augmentation limit" which was introduced by Van Slyke and his colleagues[1 2] represents the rate of excretion of urine at which the rate of excretion of urea is maximal. However, inspection of the original data on which this conception was based suggests that every increase in the rate of excretion of urine is associated with some rise in the rate of excretion of urea, and it seems fair to say that later authors[3–6] have abandoned the idea of an "augmentation limit": it is a simplification which has been convenient in the clinical application of the urea clearance test. Six results were obtained by Dr. Kenney on each of his subjects; the results in full would permit of comparisons with corresponding results obtained in Europeans.

It is, of course, important to consider how much significance should be attached to urea clearance obtained in a period of rapidly increasing diuresis. Finally, it is worth noting that Gokhale[6] and Srikantia and Shamanna[7] found low values for the urea clearance in Indians. Low results were also obtained by H. Fairfield Smith[8] in British prisoners in Japanese hands.—I am, etc.,

Sheffield, 11. ARTHUR JORDAN.

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Winter Vomiting Disease

SIR,—I welcome the letter of Dr. M. C. McKinnon (*Journal*, May 15, p. 1154) criticizing the use of the name "winter vomiting" for this disease. This unfortunate name suggests that climatic conditions have something to do with the matter, whereas, in fact, this disease is undoubtedly an air-borne virus infection. I have myself described an outbreak of over 313 cases,[1] and this occurred at the end of September and beginning of October, which even in this northern part of the country is not usually considered winter, and the weather conditions at the time were far from severe. Dr. McKinnon rightly draws attention to the short incubation period of this disease as compared with the much longer period for infective hepatitis. In my own outbreak, although I have had the opportunity of observing the children for more than three years since the event, I know of no case of jaundice. Another point is the abrupt onset of this disease as a contrast to hepatitis.—I am, etc.,

Accrington. R. C. WEBSTER.

REFERENCE

1 *Med. Offr*, 1953, **90**, 39.

Doctors and Technicians

SIR,—My friend Dr. J. F. Brailsford (*Journal*, May 15, p. 1152) sees the writing on the wall but misreads it. The trend of which he complains has nothing to do with the N.H.S. but must be studied against the background of social evolution. Hygeia, who, being the daughter of that respectable old G.P., Aesculapius, really ought to know better, now indulges in the most abandoned licentiousness, the latest offspring of her fecund womb being, apparently, the animal technician. The main cause of medical progress is the advance in technology. Consequently medicine itself must become more and more a technology, however deeply we may deplore the fact. Our mentors bleat *ad nauseam* that medicine is an art as well as a science, and that we must treat the whole man and not merely the diseased organ. The fact remains, however, that the fate of a patient is often decided by whether some backroom boy's burette reads 0.3 or 0.4. The backroom boy is not slow to realize his power.

The immense body of auxiliaries, the product of very efficient secondary education, is largely composed of those who, had Fate been kinder, could have entered medical schools and who would have made perfectly good doctors. These, urged by understandable ambition, and sometimes by resentment, are engaged in building parallel roads to a status equal to that which has been denied to them. Hence the claim that "the technologist has, or should have, equal status to the pathologist." Needless to say, this trend will become accentuated if the entry to medical schools is further restricted. At the same time these aspirants peck at every newcomer as savagely as barndoor fowls. This is what Messrs. A. E. Brown and F. Mather (*Journal*, April 24, p. 983) are now doing to the poor animal technician who is at the bottom rung of the ladder of diplomas, associateships, papers in journals, and annual congresses which they themselves are so successfully scaling.

Where will this end? I confidently predict that in 30 years all auxiliaries will have acquired consultant rank. The steps to this delectable consummation are not difficult to visualize. The training of auxiliaries in the last 20 years has made astonishing progress, while that of medical students has been comparatively static. Already there are some auxiliaries who hold the B.Sc. degree. Soon Ph.D.s will appear. They may, for all I know, be already with us. From this it will be but a short step to Doctors in Chiropody, Audiometry, Orthoptics, Speech Therapy, Radiography, Electro-encephalography, Medical Records, Operating Theatre Technique, and everything else. And if these, why not Doctors of Nursing? In the end the few who are not Doctors of some kind or other will hide their heads in shame. Never will so few have been so jealous of so many.

Some time ago I met a lady who had just been to a lecture given by a member of one of the auxiliary services. Her ecstasy knew no bounds. She might have been listening to the voice of God. I am afraid I could not conceal my amusement. "You shouldn't laugh," she said indignantly, "he's a great man. He talks to people at the Ministry."—I am, etc.,

Chesham. FFRANGCON ROBERTS.

SIR,—Dr. J. F. Brailsford draws attention (*Journal*, May 15, p. 1152) to a tendency in modern medicine on which others have also commented recently, and on which Dr. Ffrangcon Roberts dwells at length in *The Cost of Health*.[1] Dr. Brailsford suggests that the doctor who does little but stamp his signature on reports of work done by other people is in danger of losing both medical skill and status, and with this most would agree. It is also true that other workers now do for the doctor some tasks which he used to do for himself, but surely this is no cause for either alarm or despondency.

Modern developments in medical knowledge have resulted in the growth of aids to diagnosis and treatment, and in an abundance of specialized techniques so that no one person —however enthusiastic—could be expected to have an intimate grasp of them all. It seems to the impartial observer that the doctor or surgeon who makes wise and selective use of these various aids is benefiting himself and his patient, and is more likely to gain, not lose, clinical acumen and prestige. It is the non-use, or the indiscriminate use, of these subsidiary aids which is likely to harm both doctor and patient. The quotation made by Dr. Brailsford from the letters of two medical laboratory technicians ought not to be taken too seriously, especially out of their context. That context was a claim made in an annotation in the *Journal* of April 3 (p. 808) that "animal technicians" should be given equal status with medical laboratory technicians. When Mr. F. Mather's letter (admittedly ill-phrased) states (*Journal*, April 24, p. 984): "It would seem, therefore, to be more justifiable to state that in many respects the technologist has, or should have, equal status to the pathologist," I take him to mean "it would be as justifiable for the technologist to claim equal status with the pathologist as for animal technicians to claim equal status with the medical laboratory technologist," and no one would seriously support either claim. In any case the views of one or two medical laboratory technicians ought not to be taken as representing the views of the body of technicians nor that of the Institute of Medical Laboratory Technology. All professions, including the medical profession, have members who occasionally state views which would not be endorsed by the body corporate.

The approach to the problem posed by Dr. Brailsford is surely one of common sense. It is better that the physician or surgeon shall be free to concentrate his energies and training on the wider aspects of diagnosis and treatment than that he should dissipate his time and clinical specialty on the memorizing or performance of detailed technical procedures. He is not likely to have his status assailed because of the work performed by the various medical auxiliary professions: indeed, the effect of their work should be to increase it. Equally, it will profit nobody, least of all the clinician, to undervalue the work which is daily being performed by the medical auxiliary professions. —I am, etc.,

Godalming. W. H. VALENTINE.

REFERENCE

[1] *The Cost of Health*, 1952. London.

Seven Generations

SIR,—In the museum here is an MS. pedigree of the family of Kinneir from which the following is taken.

Walter Kinneir, surgeon, of Highworth (1671–1746) was father of Richard Kinneir (1711–1784), surgeon, of Cricklade, who was father of Richard Kinneir (1749–1813), surgeon, of Cricklade, who was father of Richard Kinneir (1787–1874), surgeon, of Cricklade, who was father of Richard Kinneir (1813–1892), M.D., M.R.C.S., L.S.A., of Cirencester, Purton, Weston-super-Mare, and Sherborne, who was father of Francis William Edward Kinneir (1858–1939), who was father of Guy Kinneir (b. 1891), M.R.C.S., L.R.C.P., now in practice. Seven generations. Can any family beat this record?—I am, etc.,

N. M. G. CARTER,
Hon. Curator, Cricklade Museum.

Standard of Anaesthetics in Britain

SIR,—My attention has been drawn to an article in the *Daily Express* of Wednesday, May 19, entitled "The Danger of Machines." This purports to report remarks made on the previous morning by Mr. Dickson Wright to a meeting of the American College of Surgeons. The article imputes a deplorably low standard of behaviour to anaesthetists in general. Its final paragraph, which mentions my own name as President of the Association of Anaesthetists, might have given the impression that I was present at the time and that Mr. Wright's remarks had my tacit approval, neither of which is true. It would not be necessary for me to refute these remarks if they had reached only those of us who are familiar with Mr. Wright's form of jocularity and who would give them the weight they deserve, but the American visitors may not be so familiar. It will be a pity if they have been left with a wrong impression of the standard of anaesthetics in this country, which is generally considered to be as high as anywhere in the world.

The effect of the article is to undermine the confidence of patients about to undergo surgical operations and can only be deplored—it is, as always, too late to undo the harm. I feel some sympathy with Mr. Wright that his light-hearted comments have received wider publicity than he intended. For the future, I feel that we should all remember that exaggeration as a humorous device is not wisely used in what is meant to be serious discussion, and, probably, never when it involves the denigration of colleagues.—I am, etc.,

GEOFFREY ORGANE,
President, Association of Anaesthetists of Great Britain and Ireland.

London, W.C.2.

Chloramphenicol for Athlete's Foot

SIR,—The only paper that has been published on the value of chloramphenicol in the treatment of fungus infections of the skin is by Robinson *et al.*[1] These investigators found a 1% or 2% ointment to be of value in controlling secondary infections in 17 cases of epidermophytosis. It may therefore be of interest to know that I have treated 25 cases of athlete's foot, and over a period of six months have had only two recurrences which have cleared up again after further treatment. The majority of these cases had suffered from the complaint for a number of years. The basis of my treatment was: (1) wash the feet with warm water only each night; (2) dry thoroughly and apply every alternate night a little chloramphenicol ("chloromycetin topical") with a small piece of cotton-wool and allow to dry; (3) no dusting powders or any other medication required; and (4) change socks daily. In most cases I have found three or four applications were sufficient to clear up the condition completely.—I am, etc.,

Glasgow. FRANCIS J. EVANS.

REFERENCE

[1] *Bull. Sch. Med. Maryland*, 1953, 38, 109.

Obituary

FRANK HOWITT, C.V.O., M.D., F.R.C.P.

The death of Dr. Frank Howitt on May 15 at the relatively early age of 59 removes a leading—indeed a pioneering—figure from the specialty of physical medicine and is a sad loss to a wide circle of professional colleagues and friends among whom he was held in unusual regard.

Frank Dutch Howitt was born on August 24, 1894, at Nottingham, and educated at Uppingham and Trinity College, Cambridge. In the first world war he served with the Royal Army Service Corps and later with the Royal Air Force. Returning to Cambridge, he took his M.A. in 1920, and graduated in medicine in 1923, proceeding M.D. two years later. He at once became attracted to physical medicine, and was appointed chief clinical assistant in the actinotherapeutic department at Guy's and physician in charge of physical medicine at the Royal Free Hospital and the Prince of Wales's General Hospital, Tottenham. Later he was appointed physician in charge of the large and important department of physical medicine at the Middlesex, and in due course he became senior physician of the Arthur Stanley Institute for Rheumatic Diseases. Within five years of qualifying he was called in by Lord Dawson of Penn to administer certain physical treatments to George V during his serious illness in 1928, and he attended the King both in London and during his convalescence at Bognor.

[*Lafayette, Ltd.*

Howitt was an active member of the British Medical Association, being honorary secretary to the Section of Dermatology at the Annual Meeting in 1927 and to the Section of Physical Medicine at the Centenary Meeting in 1932. In 1936 he was vice-president of the Section of Physical Medicine. He gave his services on several special committees of the Association. From 1932 onwards he was a member of the Practitioners of Physical Medicine Group Committee, and at the same period he took a prominent part in the consideration of proposals for the registration and training of physical treatment technicians and the training and recognition of balneological assistants. During the second world war he served in the R.A.M.C. with the rank of acting colonel in 1940 and the local rank of brigadier in 1942. He was placed in charge of the upgrading of recruits and of rehabilitation, and after the end of the war he continued to serve as senior consultant in physical medicine to the Army. He also became a director of Remploy Ltd. (the Disabled Persons Employment Corporation) and honorary adviser to the Ministry of Labour. When the Council of the B.M.A. set up a Rehabilitation Committee in 1945 Howitt served on it as a most valuable member for four years or more.

Industrial medicine and rheumatism were two of his great interests, and he was a member of the Nuffield Foundation committees on these subjects and chairman of the Research Board for the Correlation of Medical Science and Physical Education. He also served on the executives of the Empire Rheumatism Council and the Royal Institute of Public Health.

The illness which brought about his sudden end first manifested itself a year ago, but he faced the threat with splendid courage and patience, and his alert and eager mind continued at work. He might have looked forward to several more years of activity, but he could look back upon a career of high achievement, and also of great happiness, enhanced by his marriage in 1945 to Violet Norris, daughter of Alfred Leverton, to whom the sympathy of many friends will go out.

We are indebted to Dr. W. S. C. COPEMAN for the following appreciation: Frank Howitt, although popular in all of the numerous spheres of life in which, in addition to medical circles, he moved, was pre-eminently a man's man. He was gregarious, friendly, and easily approachable by his juniors. He entertained generously and elegantly, and was something of an authority on both food and wine. A dinner at his Harley Street home was always an experience. Although he became eminent in his chosen sphere of medicine, his real love was for the country life, and of recent years he spent all the time he could spare from practice at his farm in Gloucestershire. He was a first-rate tennis player and a fine shot throughout his life.

He came into prominence during the first illness of King George V, when he was invited by Lord Dawson to supervise the physical therapeutic measures which had become necessary. For this service he was appointed C.V.O. in 1929. It was characteristic of him that for several months subsequently he modestly avoided wearing the insignia, and later, if questioned about it, asserted humorously that he had been appointed "Mayor of Wigan, and was just showing the flag."

As a consultant in physical medicine during the second world war he was able to invest the subject with a far wider significance than had previously been attached to it. In this capacity he gathered round him a devoted band of juniors ("his boys") who carried his ideas into the various commands in which they later served. Much of what Howitt included under the heading of physical medicine has subsequently reverted to the provinces of social, preventive, and even general medicine, but he was successful in raising the subject from the status of a technique to that of a specialty. The conception, which he had inherited from Lord Dawson, that healthy living should be regarded as a powerful prophylactic against ill-health in later life led him to take a keen interest in the National Playing Fields Association and other similar movements.

In the Army he found great scope for the employment of his ideas in the upgrading of recruits and in the formation of rehabilitation centres where the concept of *active* convalescence was developed successfully. It was a considerable disappointment to him that these schemes proved to be less easy to apply in post-war civilian life. His friendship with the late Ernest Bevin while he was Minister of Labour, however, enabled him to exert considerable influence in the formation of industrial resettlement units, of which the chief is Egham, and other bodies such as Remploy Ltd., whose purpose is to return the defective worker to full-time productive employment.

He was an outstandingly successful Master of the Apothecaries Society, and he was at one time the vice-chairman of the Empire Rheumatism Council, in which he took a great interest.

Frank led a happy and useful life and we are all the poorer for his untimely passing.

ERIC POWELL, M.B., F.R.C.S.I., M.R.C.P.I.

The Kenya Branch of the British Medical Association has suffered a severe loss by the death while in office of its president, Mr. Eric Powell, on March 30 at the age of 36.

Willoughby Eric O'Connell Cole Powell was born in Yorkshire on May 12, 1917, the son of a doctor, but his early youth was spent with one of his uncles, Mr. George M. C. Powell, then a surgeon at Lusaka, in Northern Rhodesia. He returned to England to continue his education at Worksop College, Nottinghamshire, and from there he entered Trinity College, Dublin, where, with a grandfather, a father, and two uncles all members of the medical profession, it was hardly surprising that he should enrol as a medical student. A brilliant career at Trinity College was rewarded by the Daniel John Cunningham Medal in anatomy at the first medical examination, the John Mallet Purser Medal in physiology, biochemistry, and histology, the Professor's Prize in surgery, the Connolly Norman Medal in mental diseases, and the FitzPatrick Scholarship. He graduated in 1940 with second-class honours in the final M.B. and first-class honours in the final B.Ch. examinations. He had previously been awarded a gold medal as a moderator of exceptional merit. After graduation Powell held the appointment of house-surgeon at Sir Patrick Dun's Hospital, later becoming assistant in the ear, nose, and throat department, and for a time he was also assistant to the professor of pathology at Trinity College. Later he was appointed honorary consultant laryngologist to St. Patrick's Hospital, Dublin. He was elected F.R.C.S.I. in 1944 and M.R.C.P.I. in the following year. In 1947 he left Dublin to become ear, nose, and throat surgeon at King George VI Hospital, Nairobi. In addition, he established a private practice there and acted as surgeon to the British Military Hospital at Nairobi. As founder of the Nairobi Clinical Club he brought together once a month his colleagues in the profession, not only to discuss medical problems and to exchange views but to encourage the spirit of comradeship among them. His election as president of the Kenya Branch of the B.M.A. in January last was a tribute to the esteem with which he was regarded by his fellow members and to the ability they recognized in him. He had a variety of outside interests, being a city councillor, area commandant of the Kenya Police Reserve, and twice president of the Irish Society. As an after-dinner speaker and a performer on the piano accordion, his services were in great demand, while his love of children was particularly in evidence at the Chistmas parties at the Children's Hospital. He was happy, too, in his well-equipped workshop, where the making and repairing of surgical instruments gave him great pleasure. He married Dr. Edna G. Merrick, daughter of Dr. William Merrick, of Castleknock, Co. Dublin, in 1941, the year after they both graduated in medicine at Dublin, and she survives him, together with the three children of the marriage.

F. W. RANKIN, M.D., LL.D., P.A.C.S., F.R.C.S.

Dr. F. W. Rankin, President of the American College of Surgeons, and a former President of the American Medical Association, died at Lexington, Kentucky, on May 22, aged 67. He was a son-in-law of Dr. Charles H. Mayo, one of the founders of the Mayo Clinic. His fatal illness prevented him from presiding at the meeting of the American College of Surgeons in London last week.

Fred Wharton Rankin was born at Mooresville, N.C., on December 20, 1886, and received his medical education at the University of Maryland, Baltimore. After graduating in 1909 he held a resident post in Baltimore until 1912 and served as assistant demonstrator in anatomy and as associate in surgery at his own university from 1913 to 1916. He then joined the Mayo Clinic as assistant surgeon until 1922, when he spent a year as professor of surgery in the University of Louisville. He returned to Rochester in 1926 as associate professor of surgery at the University of Minnesota Medical School and surgeon to the Mayo Clinic. He left these posts in 1933 to practise surgery at Lexington, Kentucky, where he was appointed surgeon to St. Joseph's Hospital, a position he held at the time of his death. Since 1941 he had been clinical professor of surgery at Louisville.

Rankin contributed much to the literature on clinical surgery, and was an internationally known authority on the surgery of the colon and rectum. His monograph on the *Surgery of the Colon* appeared in 1926, and he was also the joint author of *The Colon, Rectum and Anus* (1932), and *Cancer of the Colon and Rectum* (second ed., 1950).

During the last war he served as chief consultant to the Surgeon-General, U.S. Army, with the rank of brigadier-general. The American Medical Association in 1945 awarded him its Distinguished Service Medal for his meritorious services in this appointment. He was president of the Southern Surgical Association in 1937, the American Medical Association in 1942, the American Surgical Association in 1949, and the American College of Surgeons at the time of his death. In 1953 Rankin was awarded an honorary fellowship of the Royal College of Surgeons, and during the recent meeting of the Association of Surgeons of Great Britain and Ireland, attended by many distinguished members of the American College of Surgeons, the University of Leeds conferred upon him the honorary degree of LL.D.

Dr. E. WELLISCH died in hospital at Dartford, Kent, on March 11, after a short illness. Erich Wellisch was born in Vienna on January 21, 1898, the son of a high official of the municipality who made a name for himself by becoming an authority on blood groups after his retirement. To emulate his father's distinction was Erich Wellisch's fondest ambition. He graduated M.D. at the university of his native city in 1924. After a period of postgraduate study in neurology, he specialized in physical medicine and soon became an authority on light therapy. A monograph on this subject and a number of publications on the physiotherapy of neuritis and dermatitis bear witness to his great abilities as a clinical observer and to his therapeutic resourcefulness. Having had to leave Vienna in 1938, Dr. Wellisch started afresh in this country, taking the Conjoint Diploma in 1941. He took up psychiatry, and acquired the D.P.M. of the English Royal Colleges in 1945. With the seriousness and enthusiasm so characteristic of him, he specialized in child psychiatry, and from 1947 to his death was in charge of the Crayford Child Guidance Clinic at Bexleyheath, Kent.

Dr. E. STENGEL writes: Dr. Wellisch was a hard worker who did not spare himself. He succeeded in combining clinical and research work. He undertook a series of investigations into the application of projection tests in child guidance, and his papers on the Rorschach test were notable contributions in a field full of controversy. Other publications dealt with eye manifestations in maladjusted children, follow-up investigations in child guidance work, and dreamy states. Only a few months before his death he completed a book entitled *Isaac and Oedipus*, in which

he analysed the ancient Hebrew legend of the sacrifice of Isaac side by side with the Greek tragedy. Dr. Wellisch was deeply interested in the philosophical foundations of psychiatry. Had he lived he would undoubtedly have added to his achievements as a clinician and scholar. The sympathy of his friends and colleagues goes out to his widow and his two children.

Dr. V. E. BADCOCK, one of the best known and most respected medical practitioners in rural north Northumberland, died at his home near Cornhill-on-Tweed on April 6 at the age of 69. Vincent Edgar Badcock had a distinguished career as a student at Durham University, where he graduated M.B., B.S. in 1906, proceeding to the M.D. three years later, when he was awarded a gold medal for his thesis. After graduation he held resident appointments at the Royal Victoria Infirmary, Newcastle-upon-Tyne, and for a time he was assistant demonstrator in anatomy in the university. In 1909 he became assistant to the late Dr. Alexander Dey, of Wooler, and in the following year succeeded to the practice of Dr. W. H. Shand at Flodden Lodge, near Cornhill, and entered into partnership with Dr. Dey. In the first world war Dr. Badcock joined the R.A.M.C. and served with distinction in France as a regimental medical officer, being awarded the Military Cross for conspicuous gallantry in attending to the wounded when he himself was severely wounded in the foot. He would not have his wounds attended to until everyone else had been treated, and as a result his condition became worse. After numerous operations his leg was amputated below the knee. He returned to his extensive practice in a scattered rural district and was regarded in very high esteem by countrymen in all grades of society. He was beloved and trusted by his patients, and his colleagues in the profession found in him an honourable and delightful friend. In 1921 he was elected chairman of the North Northumberland Division of the B.M.A.; he was also a member of the executive and ethical committee for a number of years, and a regular attendant at divisional meetings as long as his health permitted. During the last war he was chairman of the local medical war committee and took a special interest in the protection of practices scheme and in the arrangements for the medical attention of evacuees in the area. Dr. Badcock was a keen cricketer and played regularly for the Tillside club, of which he became chairman. In his later years he rarely missed being present at a match on the delightful ground at Etal near his home. He was a bachelor and is survived by two brothers and several nieces and nephews. One of his nephews, Dr. Alan Bousfield, had been in partnership with him for some years, and will carry on the practice at Flodden Lodge.—D. T. McD.

Dr. R. S. DE BRUYN, who was on the surgical staff of the Stamford and Rutland Hospital, died at Capetown, South Africa, on May 6 at the age of 56. Robert Saunders de Bruyn, who was born on July 14, 1897, served in the Royal Flying Corps in the first world war and was awarded the D.F.C. in 1919. Soon after demobilization he enrolled as a medical student at Guy's Hospital, qualifying M.R.C.S., L.R.C.P. in 1927, taking the diploma of L.D.S. of the Royal College of Surgeons of England in the same year. After qualification he held a number of appointments at Guy's Hospital before settling in practice at Stamford in 1932, the year in which he was admitted F.R.C.S.

We are indebted to Dr. E. C. TILL for the following appreciation: The untimely death of Robert Saunders de Bruyn on May 6 is a grievous and irreplaceable loss both to his colleagues and to the community he served so ably for 20 years. His stature in general surgery was such that he was most unfortunate in not securing a staff appointment at Guy's. After a period spent as surgical registrar and some months in the U.S.A., he joined a firm of general practitioners at Stamford as a surgical partner, and in 1932 came on to the staff of the Stamford and Rutland General Infirmary. It was typical of his wide interests in medicine that, until the rapidly expanding volume of his surgical work made it impossible, he undertook and enjoyed a fair amount of general practice. During the last war he laboured for six years, virtually without any holiday or respite, and achieved a truly remarkable volume of major surgery at his hospitals at Stamford and Holbeach. After the commencement of the National Health Service, he relinquished his partnership and continued consultant appointments with the East Anglian and Sheffield Regional Hospital Boards. In July, 1953, after some weeks of increasing unfitness, he submitted to lengthy investigations which terminated in an abdominal operation. His death at Capetown occurred as the result of a relapse while on convalescent holiday. Much of his professional success lay in his judgment, which was rarely at fault. Strongly individualistic and endowed with a fine memory for faces and events, he had that rare quality of so shouldering his patients' burdens that all worry and tension vanished with his advent. His rich personality did not suffer fools gladly, and his lambent wit flickered impartially upon all and sundry according to their deserts. Essentially a man of simple tastes, he enjoyed good music, literature, and the arts. He bore the considerable travail of his long illness with great fortitude, much aided by the devoted care and encouragement of his wife, to whom we offer all our sympathy in her great loss.

Mr. W. E. SPRINGFORD, consulting surgeon to the Charing Cross Hospital unit at Mount Vernon Hospital, Northwood, died at his home at Northwood on May 18 at the age of 41. William Edmund Springford was born on November 29, 1912, and received his medical training at Charing Cross Hospital, graduating M.B., B.S. from London University in 1936 and winning the Governor's Clinical Gold Medal at the hospital in the same year. He obtained the F.R.C.S. in 1941, and in the following year he was awarded the J. H. Morgan Surgical Prize at Charing Cross Hospital. After graduation he held the appointment of house-surgeon at his own teaching hospital, later becoming resident surgical officer at the Chesterfield and North Derbyshire Royal Hospital and at the Kent and Sussex Hospital, Tunbridge Wells. On the outbreak of war in 1939, Mr. Springford, who was then in practice at Snaresbrook, entered the Emergency Medical Service and worked at Ashridge Hospital, Berkhamsted, until 1944, when he joined the R.A.M.C. as a lieutenant. Ill-health, however, compelled him to relinquish his commission in 1947, by which time he had attained the rank of major as a surgical specialist. Soon after his return to civilian life, Mr. Springford was appointed surgical specialist at Northwood, later becoming consulting surgeon to the Royal Masonic Institute for Girls.

T. D. L. writes: Mr. W. E. Springford was without doubt one of the nicest consultants we in this area have ever known. He was ever ready with good advice and never let a practitioner down. His good humour and charm delighted our patients, and these qualities, with his sound surgery, made us happy to consult him. Those of us who were privileged to observe the remarkable courage shown by him and by Mrs. Springford towards the end have had an object lesson in dignity and fortitude. To Mrs. Springford we extend our deepest sympathy. We shall miss him much.

Dr. C. H. R. PENTREATH, who was 81 years of age, died in hospital in Nairobi on May 19, four days after he had been savagely and senselessly attacked by Mau Mau terrorists. He left his home on May 15 to buy some cigarettes at a near-by inn, when he was bludgeoned by a terrorist in a country road near Nairobi, and left in a semi-conscious state on the roadway. Charles Henry Reginald Pentreath was born at Exmouth, Devon, on October 1, 1872, and was educated privately and at Cambridge University, where he took the Natural Sciences Tripos in 1892. Four years later he obtained the degrees of M.B., B.Chir., having received his clinical training at St. Mary's Hospital. He spent much of his professional life abroad. In 1900 he was resident medical officer at the Auckland General Hospital in New Zealand, and from 1902 to 1905 resident

medical superintendent at the Government Sanatorium at Cambridge, New Zealand. In 1911 he returned to England, and at the outbreak of war in 1914 was in a partnership at Maidenhead, where he was also surgeon to the local cottage hospital. He served in the R.A.M.C. from 1914 to 1916, and then went to live in Devonshire, where he was oculist to the Devon County Council. From 1918 to 1920 he was a medical adviser to the Ministry of Pensions. Soon after the end of the first world war he went abroad again, this time to Nairobi, where he was in practice as an ophthalmic specialist until 1947, when he retired.

Medical Notes in Parliament

Prescribing Cortisone and A.C.T.H.

Mr. A. BLENKINSOP (Newcastle-upon-Tyne, East, Lab.) asked the Minister of Health whether, under his regulations, cortisone and A.C.T.H. could be prescribed by doctors to their private patients. Mr. IAIN MACLEOD stated on May 20 that there were no regulations governing the prescription of these or any other drugs for the use of private patients. In the public interest he had limited the distribution of cortisone and A.C.T.H. to selected hospitals, from which they might be obtained for the treatment of private patients suffering from certain serious conditions.

Mr. BLENKINSOP said it was undesirable that patients should feel that they could get these things as private patients but might not be able to get them, at any rate from general practitioners, under the Health Service. Would he urge on doctors generally that these drugs should not be prescribed except in hospitals? Mr. MACLEOD said that distribution was limited to about 100 selected hospitals. The supply position was rapidly becoming a great deal easier, and it was hoped to extend the distribution very considerably. Obviously cortisone could not be denied to a patient merely because he happened to be in a private room and not in a ward.

Mr. T. WILLIAMS (Don Valley, Lab.): Before a general distribution of cortisone is made, will the Medical Research Council be consulted on how, by whom, and in what quantities it shall be prescribed? Mr. MACLEOD: Certainly. As cortisone becomes increasingly available this sort of problem will arise. We shall move in step with the Medical Research Council.

Dr. EDITH SUMMERSKILL (Fulham, West, Lab.) asked the Minister to make it clear that if a hospital doctor thought a Health Service patient would benefit from the drug he would be able to prescribe it. Mr. MACLEOD replied that he was not certain that he could give precisely that assurance yet, but the time was rapidly approaching when supplies would be fully adequate to fulfil all such purposes.

Chloramphenicol Treatment

Mr. IAIN MACLEOD told Dr. BARNET STROSS (Stoke-on-Trent, Central, Lab.) on May 20 that information was not available about the number of deaths resulting from treatment by chloramphenicol. Dr. STROSS asked whether it was fair to say that this powerful and most useful drug should only be used for children if other drugs were not available or would not do the work. Mr. MACLEOD replied that that was not a matter on which a layman should pronounce. Certainly considerable dangers were involved in the use of the drug, and there had been a number of deaths—most of them due to an overdose being given.

Trichinosis from Sausage Meat

Mrs. E. BRADDOCK (Liverpool, Exchange, Lab.) asked the Minister of Health if his attention had been drawn to the recent outbreak of trichinosis in Liverpool; and what action he had taken to make it fully known that this infection was caused by eating raw pork sausage meat. Mr. IAIN MACLEOD replied on May 20 that the medical officer of health of Liverpool reported a localized outbreak of trichinosis there last November, and at the time warned the public through the local and national press not to eat uncooked pork or pork sausage meat. Only three small outbreaks in England and Wales, of which this was one, had been reported in the past seven years. No further action on his part was called for. He did not dissent from Mrs. Braddock's further point that, although there had been only a few localized outbreaks, the danger existed and people should be made aware of it. The danger, he said, was in eating raw sausage meat as if it were meat paste.

Sale of Calomel

Mr. S. SWINGLER (Newcastle-under-Lyme, Lab.) asked the Home Secretary if, in view of public anxiety caused by the recent deaths of infants attributed to the presence of calomel in teething powders administered to them, he would state the grounds on which the Poisons Board had advised him against controlling the sale of calomel and request the Board to reconsider the matter. Sir DAVID MAXWELL FYFE, replying on May 20, declined, pointing out that the proceedings of the Poisons Board, the advisory committee set up by the Pharmacy and Poisons Act, 1933, were confidential.

Practice Loans in Scotland

Miss M. HERBISON (Lanarkshire, North, Lab.) asked the Secretary of State for Scotland on May 18 how many applications had been received from practitioners for an interest-free loan to establish group practices; and from which districts in Scotland they had originated. Commander T. D. GALBRAITH, Under Secretary, informed her that applications had been received from 18 groups of doctors in Edinburgh, Glasgow, Ayrshire, Fife, Lanarkshire, the Lothians, and Stirlingshire. Miss HERBISON asked how soon a decision would be given; and whether, as so many applications had been received in such a short time, "the miserable £100,000" would be sufficient to meet them. Commander GALBRAITH said the applications would have to be gone into before it could be decided which groups should get the first sums available. It might take some little time before a final decision was made.

Old People in Mental Hospitals

Mrs. JEAN MANN (Coatbridge and Airdrie, Lab.) asked how far it was the practice, when there is a shortage of beds in general hospitals, for old persons to be given accommodation in mental hospitals; and to what extent they were required to be certified, on refusing, in these circumstances, to enter voluntarily. Commander T. D. GALBRAITH said the Secretary of State was not aware of any such practice. Some forms of senile mental illness could be cared for properly only in a mental hospital; and where admission as a voluntary patient was not accepted, certification might be the only way of securing that the patient got the care and treatment needed. Mrs. MANN said there was widespread belief in industrial areas that old people were being put into mental hospitals because there were insufficient beds in general hospitals, and that when the old people protested and did not go voluntarily they were certified. Commander GALBRAITH said that if she would give him details he would look into them.

Mrs. MANN also asked if it was now permissible under regulations to certify elderly patients entering mental institutions as suffering from mental senility; and how far deviation from the words laid down by statute was permitted. Commander GALBRAITH stated that the conditions to be met before a person could be certified were laid down by statute, as also were the terms in which the relative certificates must be given. There was no power to permit any deviation, such as that suggested, from the terms and conditions laid down by statute.

Pay-beds in Scotland

Commander GALBRAITH stated in answer to Mr. W. HANNAN (Glasgow, Maryhill, Lab.) that during the year ended March 31, 1953, on an average less than a quarter of the pay-beds in Scottish Health Service hospitals were unoccupied. There were 913 such beds, or 1½% of all staffed

beds. The percentage occupancy of these beds was about 75, compared with 83½ for all the beds in hospitals. This was considered to be quite a high percentage.

Mau Mau Psychology

Mr. C. ALPORT (Colchester, Con.) asked the Secretary of State for the Colonies on May 19 whether the Government would appoint a technical group to inquire into the anthropological and psychological aspects of the Mau Mau outbreak. Mr. H. HOPKINSON, the Minister of State, replied that in February the Kenya Government invited Dr. J. C. Carothers, a psychiatrist with a number of years' experience in Kenya, to carry out a special investigation into the psychology of Mau Mau. He completed his report last month. Until this had been examined he could not say what further steps would be required.

M.P.'s Salaries

On May 24 Members of Parliament voted by 280 votes to 166 to raise their salary from £1,000 to £1,500 a year. This is two and a half times the 1939 salary of £600, and one and a half times the 1946 salary of £1,000.

Hospital Appointments Advertising.—Replying to Dr. A. D. D. BROUGHTON on the cost to the National Health Service for advertising to invite applications from medically qualified men and women for hospital appointments, Mr. IAIN MACLEOD said that complete information was not available, but the expenditure of all regional hospital boards and hospital management committees in England and Wales, and half the boards of governors, during the year ending March 31, 1953, was £191,000.

Birmingham Patients Waiting.—The Minister of Health has informed Mr. S. T. SWINGLER (Newcastle-under-Lyme, Lab.) that at the end of March there were 4,512 patients awaiting admission for gynaecological treatment at hospitals in the Birmingham region.

School Medical Service.—The Prime Minister, answering a question by Miss IRENE WARD (Tynemouth, Con.), said he was advised that it would not be desirable at present to transfer responsibility for the school medical service to the Minister of Health.

Striede Knee-joint Experiments.—Mr. IAIN MACLEOD has informed Lieutenant-Colonel M. LIPTON (Brixton, Lab.) that experimental tests of six Striede knee-joints were in progress, but no final decision had been reached. Experiments had been going on for just over a year.

Universities and Colleges

UNIVERSITY OF CAMBRIDGE

Dr. E. D. Adrian, O.M., P.R.S., Master of Trinity College, has been appointed a manager of the E. G. Fearnsides Fund until December 31, 1956, and a governor of the Darwin Trust until July 30, 1958.

The following reappointments are announced: Dr. F. G. J. Hayhoe as University Lecturer in the Department of Medicine from March 1, 1954, to the retiring age; Dr. J. R. Robinson as an Assistant Director of Research in the Department of Experimental Medicine from October 1, 1954, for five years; Dr. W. A. Fell as an Associate Lecturer in Physical Medicine in the Department of Medicine from April 1, 1954, to the retiring age or for so long as he remains a consultant in physical medicine to the United Cambridge Hospitals, whichever period is the shorter.

Mr. J. H. Doggart has been appointed representative of the University at the seventeenth International Congress of Ophthalmology to be held at Montreal and New York in September, 1954.

Dr. G. H. Wright has been reappointed University Lecturer in the Department of Anatomy, and Dr. G. R. E. Naylor University Lecturer in the Department of Pathology, both with tenure from October 1, 1954, to the retiring age. Dr. P. A. G. Monro has been reappointed University Demonstrator in the Department of Anatomy, and Dr. T. S. L. Beswick University Demonstrator in the Department of Pathology, both with tenure from October 1, 1954, for two years.

Dr. Raymond Williamson has been appointed representative of the University at the International Congress on the History of Medicine to be held in Italy in September, 1954.

Dr. S. D. Elliott has been appointed an Assistant Director of Research in the Department of Animal Pathology with tenure from July 1, 1954, for five years.

Dr. J. A. Hislop has been elected to an Elmore Medical Research Studentship from January 1, 1954.

In Congregation on January 23 the following degrees were conferred:

M.D.—W. M. Keynes, O. H. Wolff, W. H. Simonds, B. Schofield.

M.B., B.CHIR.—H. H. Shawdon, *L. Wilkinson, D. E. Corlett, R. H. Morgan, H. J. Wood, R. D. France, *C. P. D. Tong, *H. Eaton, F. McP. Low, *Ee Keng Lee.

M.B.—*J. D. Avison, D. K. Robinson, *G. P. Vaughan, R. C. Benians, G. N. Penlington, *H. M. Buckland, C. W. M. Cooper, *I. M. Allison, *L. R. L. Burton, *J. G. Pritchard, *G. A. Reed, *G. McC. Grandsen, *B. I. F. Eminson, *S. R. Laing, M. J. Purves, *E. S. Reed, *F. S. Cozens, *J. L. Tasker, M. C. G. Mantell, R. E. Williams, Mrs. Jane F. Mackworth, *E. Moran, *L. Weiss.

In Congregation on February 5 the following degrees were conferred:

M.D.—J. F. P. Skrimshire.

M.B., B.CHIR.—*A. M. Hammerton-Fraser, *D. W. Bentinck.

M.B.—*I. Oswald, J. R. T. Finlayson.

In Congregation on March 20 the following degrees were conferred:

M.CHIR.—*J. F. Bolton Carter, *A. G. Dingley, A. Standeven.

M.B., B.CHIR.—*A. J. Danby.

M.B.—A. D. Thursz.

*By proxy.

The following candidates have been approved at the examinations indicated:

FINAL M.B.—*Part II ([3]Principles and Practice of Physic, [3]Surgery, [4]Midwifery and Gynaecology)* (the figures indicate the section or sections passed): [2 3 4]I. M. Allison, [4]J. D. Avison, [4]S. G. Bayliss, [2 3 4]R. C. Benians, [2 3 4]G. F. B. Birdwood, [2 3 4]R. J. Blow, [3]J. A. D. Briggs, [2 3]L. F. Brunt, [3]H. M. Buckland, [2 3 4]G. L. Bunton, [2 3]D. C. L'E. Burges, [3]L. R. L. Burton, [2 3 4]D. J. Buttery, [3 4]W. H. Carling, [2 4]Mrs. A. Clarke, [2]D. M. T. Cones, [3 4]C. W. M. Cooper, [3]D. E. Corlett, [3 4]F. S. Cozens, [3]J. L. Crammer, [2 3 4]J. Crook, [2 3]Mrs. E. J. P. Davies, [4]M. W. L. Davis, [2]A. E. L. de Thierry, [3]J. P. Dickson, [3]D. G. Dingle, [2 3 4]P. M. Dunn, [2 3 4]H. Eaton, [3]Mrs. E. A. Eldon, [3]B. I. F. Eminson, [3]J. P. English, [3]J. Fairley, [3]J. R. T. Finlayson, [2 3]N. W. Fogg, [3]R. H. Gibbon, [3]J. T. Gibbs, [3 4]P. Gortvai, [2 3]Mrs. M. H. P. Gregory, [4]A. M. Hammerton-Fraser, [3 4]J. W. Harding, [3 4]M. E. Hern, [4]F. Heyes, [2 3 4]G. H. Hilton, [3]B. Holt, [3]M. Horowitz, [3]L. H. Hurrell, [2 3 4]H. Jacobs, [3]P. O. Jones, [3]F. E. Kenyon, [4]R. J. Knight, [3]S. R. Laing, [2 3 4]R. C. Lawson, [2 3 4]E. K. Lee, [3]S. P. Lock, [2 3 4]F. M. Low, [4]C. M. McGregor, [2 3]R. F. McKnight, [2 4]Mrs. J. F. Mackworth, [4]J. R. McNeill, [4]M. C. G. Mantell, [3 4]H. C. Masheter, [4]G. F. Mayall, [2 3]J. S. Miller, [3]E. J. Mitchell, [2]M. T. Moore, [2 3 4]E. Moran, [2]R. H. Morgan, [2 3 4]N. H. Moynihan, [2]J. C. Newell Price, [3]I. Oswald, [2 3 4]C. J. Pattinson, [3]A. B. L. Peake, [4]J. G. Pritchard, [4]M. J. Purves, [3]E. S. Reed, [2 3]G. A. Reed, [3]D. K. Robinson, [3]J. O. Robinson, [3]Mrs. L. M. Rochelle, [4]J. D. Salmon, [4]J. R. Scott, [3]H. H. Shawdon, [3]P. T. Smith, [3]J. K. Snell, [2 3]G. P. Starck, [4]I. G. Tait, [4]J. L. Tasker, [3 4]A. D. Thursy, [2 4]S. A. Tillyard, [2 3 4]C. P. D. Tong, [4]D. E. Tunnadine, [4]G. P. Vaughan, [4]J. D. S. Vernon, [3 4]J. A. A. S. Webber, [4]J. H. H. Webster, [2 3 4]L. Weiss, [4]P. D. W. Wickenden, [4]L. Wilkinson, [3]R. E. Williams, [3]R. V. F. Williams, [3 4]W. D. W. Williams, [2]W. A. Williamson, [2 3]H. J. Wood, [4]J. R. Wood, [4]S. M. Worrall. *Part I (Pathology and Pharmacology):* D. P. Addy, R. W. Ainsworth, I. R. Aldous, D. L. Almond, J. Anderson, P. C. Anderson, P. C. W. Anderson, W. Atherton, D. W. Atkinson, J. Bamforth, R. B. Bennet, D. W. Bentinck, G. D. Blackledge, J. R. Blatch, J. W. Blaxill, L. H. Blonstein, J. N. Bodger, A. Bracewell, J. P. Brady, P. Brine, M. E. Budleigh, G. L. Bunton, E. Burkinshaw, P. J. Burrows, N. R. Burt, J. R. Burwell, S. T. G. Butterworth, P. G. T. Bye, D. H. Cameron, W. H. Carling, G. G. Carmichael, R. A. Carpenter, R. A. Carter, S. B. Carter, T. D. Carter, J. D. Chard, E. B. Clayton, T. R. Clendon, J. R. Cobbett, W. L. Cordeaux, M. Cornelius, I. J. Cour-Palais, E. E. Denman, P. A. Dinkel, B. H. S. Dixon, W. D. Dolton, H. Dovey, P. A. Eckstein, J. D. Ellis, J. M. Evans, D. K. Fairweather, D. T. Finlay, J. T. Fitzsimons, R. D. France, A. M. Freeman, J. S. Garfield, F. E. Garrad, E. F. D. Gawne, A. E. Gibbs, A. E. R. Gibbs, R. K. Gilbert, G. McC. Gransden, C. M. B. Grigson, J. N. Harcourt-Webster, R. J. Haythornthwaite, M. E. Hern, C. P. Hindley, B. Holt, J. H. C. Hunt, L. H. Hurrell, R. D. Hyde, R. B. Jenkins, F. L. Johnstone, D. H. Jones, P. J. D. Kirk, W. G. R. M.

Laurie, E. P. Lawrence, J. A. S. Lees, M. J. Littlewood, I. V. Longfield, R. D. Lowe, R. S. McKim, I. E. McLaren, S. M. Madeloff, R. Malley, J. W. Maltby, P. B. C. Matthews, K. L. G. Mills, C. J. Moore, C. B. Mortimer, J. F. Mowbray, M. T. C. Mower, M. A. Newland, W. S. Ogden, A. M. Parfitt, R. W. Payne, R. J. C. Pearson, G. N. Penlington, M. R. K. Plaxton, A. Pollard, D. J. H. Prosser, M. J. Purves, J. C. L. Rawes, J. N. Rea, E. Redfearn, S. E. Reed, D. J. Roberts, I. R. Robertson, A. Robinson, B. H. B. Robinson, I. Ross Russell, A. O. Russell, J. R. Scott, G. G. Scott-Brown, R. O. Selby, P. R. Shires, R. G. D. Small, G. C. Spackman, J. A. Stamford, L. M. Stauffer, R. M. Stirland, F. Summers, E. I. Tanner, G. J. M. Thompson, J. E. Trapnell, J. C. S. Turner, A. S. Valentine, I. H. M. Veitch, J. F. Walker, C. A. M. Walkley, R. S. Wardle, N. A. Waring, J. R. C. Weatherly, D. N. Whitmore, B. M. Wild, J. C. Willan, J. T. N. Williams, R. E. Williams, W. A. Williamson, J. F. Wood, B. Woods.

M.CHIR.—J. W. Bolton Carter, A. G. Dingley, A. Standeven, J. S. W. Whitehead.

The following degrees were conferred on February 20:

M.D.—D. Ainslie, R. J. Harrison, P. H. Mitchell, A. L. Furniss.

M.B.—P. T. Smith (by proxy), C. J. Pattinson, S. M. Worrall.

UNIVERSITY OF LONDON

Dr. J. P. Collard has been elected and Dr. A. Talbot Rogers re-elected as two of the representatives of the Faculty of Medicine on the Standing Committee of Convocation for three years from January 9, 1954.

Professor J. M. Mackintosh has been nominated for re-appointment as representative of the University on the governing body of the Slough Industrial Health Service.

Mr. J. M. Pullan has been recognized as a teacher of surgery in the University at St. Thomas's Hospital Medical School.

UNIVERSITY OF MANCHESTER

The Council of the University has approved the following changes in status of members of the staff, to take effect, except where otherwise indicated in parentheses, from September 30, 1954: *To be Reader in the subjects named: Surgery,* Mr. R. P. Jepson; *Social Medicine,* Dr. R. F. L. Logan (from March 1, 1954). *To be Senior Lecturer in the subject named: Ophthalmology,* Dr. Alan Stanworth (from a date to be approved). *To be Lecturers in the subjects named: Pathology,* Dr. J. C. Burne, Dr. G. E. Paget, Dr. J. P. Smith; *Neuropathology,* Dr. P. O. Yates (from October, 1953). *To be Assistant Lecturers in the subject named: Pathology,* Dr. H. de C. Baker, Dr. B. L. Williams.

The following candidates have been approved at the examination indicated:

DIPLOMA IN PSYCHOLOGICAL MEDICINE.—*Part II:* D. L. Fox, K. Rawnsley.

UNIVERSITY OF LIVERPOOL

The degree of Ph.D. in the Faculty of Medicine has been granted to T. G. Richards, M.D.

The following diplomas have been awarded:

D.M.R.(D.).—*Part I:* H. J. J. Beyleveld, A. Bhattacharya, H. E. Jones, J. P. Murray, I. P. Smyth.

D.M.R.(T.).—*Part I:* B. Roy.

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW

At a meeting of the Faculty held on March 1, with Dr. Andrew Allison, President, in the chair, N. Radhakrishnan was admitted a Fellow of Faculty *qua* physician; on May 3 S. G. McAlpine was also admitted a fellow of Faculty *qua* Physician.

ROYAL COLLEGE OF SURGEONS IN IRELAND

On April 2 the Fellowship of the College was conferred on D. F. Doherty, J. Kyle, J. G. Maher.

The following diplomas have been awarded:

D.C.H.—B. P. K. Ryan, J. B. Shea.

D.O.M.S.—R. E. Tingey.

D.P.M.—E. Casement, A. C. Fleming, J. P. F. Fogarty, P. J. Meehan, D. C. Hutchison, K. A. McDaid, R. R. Steinert.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

At a meeting of the Council of the College held on January 30, with the President, Mr. Arthur A. Gemmell, in the chair, the following were elected to the Membership: G. T. D. Barr, D. J. Cassidy, Vivienne A. Croxford, H. F. Daghistany, P. J. Dwyer, A. L. T. Easton, D. W. S. Gordon, T. P. Grant, J. Greenwell, K. Greig, R. W. Hughes, G. A. Humphreys, P. D. C. Jackson, K. B. Layton, C. V. Love, A. C. McInnis, P. Manolis, M. Mukerji, F. A. Murray, R. F. O'Donoghue, G. D. Pinker, D. E. Savage, S. G. Singh, H. J. Tighe, J. R. D. Tomlinson, A. C. Turnbull, R. Vaish, P. S. Watson, V. T. White.

CONJOINT BOARD IN SCOTLAND

The following candidates, having passed the final examinations, have been granted the diploma of L.C.R.P.Ed., L.R.C.S.Ed., L.R.F.P.&S.G.: H. C. Carver, T. K. Chetty, J. B. Collinson, P. T. Huppert, G. C. H. Knight, A. B. Masters, E. P. McKay, J. M. Nichols, A. I. Y. Orr, M. P. Pather, A. Pribyl, Katalin E. Schopflin, F. Shoucair, S. A. Singh, V. Vahala, J. Vitolins.

FACULTY OF RADIOLOGISTS

At the examination for the Fellowship of the Faculty held in November, 1953, the following satisfied the examiners:—*Radiotherapy:* F. M. Benton, D. M. T. Cones, G. M. King, W. D. Rider; *Radiodiagnosis:* K. E. Jefferson, K. A. Rowley, P. W. E. Sheldon.

Vital Statistics

Week Ending May 15

The notifications of infectious diseases in England and Wales during the week included pneumonia 463, scarlet fever 898, whooping-cough 2,660, diphtheria 9, measles 1,706, dysentery 1,031, acute poliomyelitis 19, paratyphoid fever 7, and typhoid fever 3.

Infectious Diseases

Increases in the number of notifications of infectious diseases in England and Wales during the week ending May 8 included 189 for dysentery, from 759 to 948, 148 for whooping-cough, from 2,233 to 2,381, and 96 for scarlet fever from 623 to 719, while the only decrease of any size was 236 for measles, from 1,970 to 1,734.

The 9 cases of diphtheria notified were 3 fewer than in the preceding week and the smallest number ever recorded. 4 of the 9 cases were notified in Liverpool C.B. The largest variation in the local trends of scarlet fever was a rise of 31 in Yorkshire West Riding, from 44 to 75. The largest fluctuations in the returns of whooping-cough were a rise of 53 in Kent, from 149 to 202, and a fall of 47 in Warwickshire, from 169 to 122. The only large decline in the incidence of measles was 144 in Norfolk, from 326 to 182. The number of notifications of paratyphoid fever rose from 3 to 13.

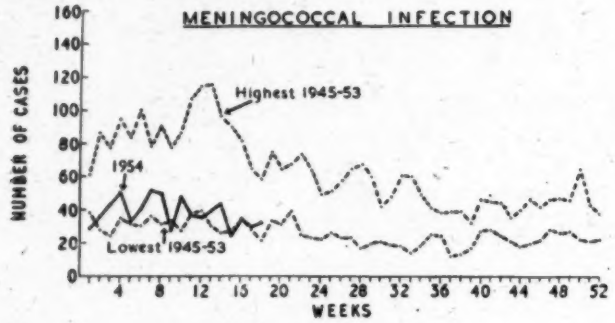
23 cases of acute poliomyelitis were notified during the week; these were the same for paralytic and 3 more for non-paralytic cases than in the preceding week. Two cases were notified in Leeds C.B., Sunderland C.B., and Lancaster M.B.

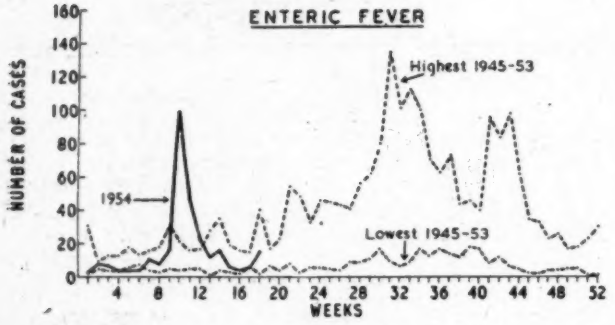
The largest rise in the notifications of dysentery was 119 in Lancashire. The largest returns were Lancashire 262 (Denton U.D. 54, Swinton and Pendlebury M.B. 31, Liverpool C.B. 23, Irlam U.D. 23, Manchester C.B. 19, Salford C.B. 13, Golborne U.D. 12, Blackpool C.B. 10, Bolton C.B. 10), Yorkshire West Riding 118 (Dewsbury C.B. 45, Bradford C.B. 13, Sheffield C.B. 10), London 107 (Islington 42, Lewisham 12, Hampstead 11), Middlesex 57 (Tottenham M.B. 22), Leicestershire 47 (Leicester C.B. 40), Kent 30 (Sevenoaks R.D. 25), Essex 29, Nottinghamshire 28 (Nottingham C.B. 21), Sussex 26 (Brighton C.B. 11), Cheshire 25 (Stalybridge M.B. 13), Warwickshire 25 (Birmingham C.B. 23), Glamorganshire 24 (Llwchwr U.D. 11), and Surrey 23.

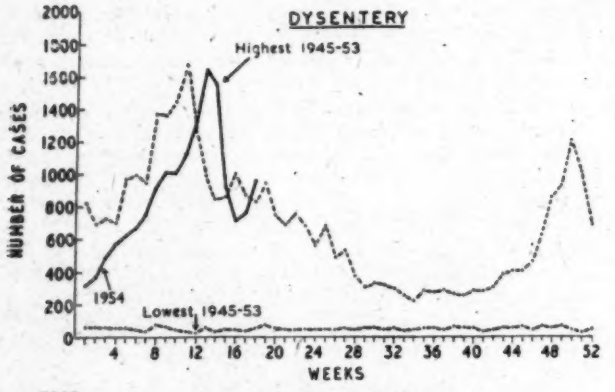
In Scotland the number of notifications of dysentery increased by 31, from 280 to 311. The rise was due to the outbreak in Glasgow, where the cases rose from 178 to 220.

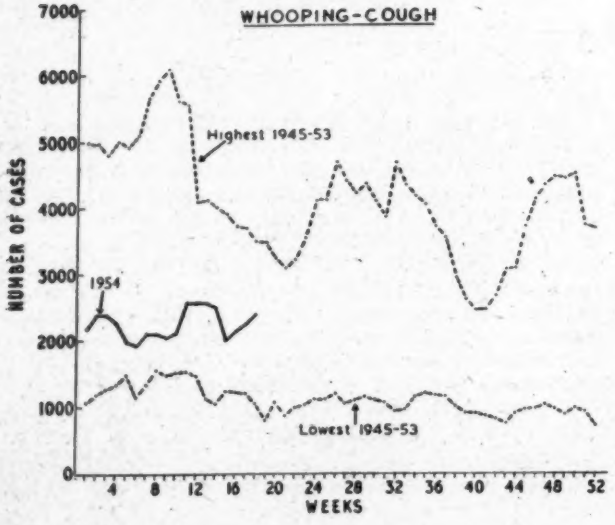
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1945–53 are shown thus - - - - - -, the figures for 1954 thus ————. Except for the curves showing notifications in 1954, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **May 8** (No. 18) and corresponding week 1953.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1954					1953				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	9	0	3	0	1	22	1	10	0	2
Dysentery	948	107	311	3	4	729	80	90	1	1
Encephalitis, acute	5	0	0	0		0	0	3	0	
Enteric fever:										
Typhoid	2	1	1	0	0	1	0	3	1	
Paratyphoid	13	0	1	0	0	14	1	0	0	
Food-poisoning	231	102				137	25		0	
Infective enteritis or diarrhoea under 2 years				13	23				12	10
Measles*	1,734	71	201	108	331	9,809	369	359	262	195
Meningococcal infection	32	2	11	1	2	37	1	15	2	
Ophthalmia neonatorum	32	1	10	1		46	?	3	2	
Pneumonia†	506	23	183	10	2	479	15	219	6	2
Poliomyelitis, acute:										
Paralytic	15	2	2	0	0	28	4	1	1	3
Non-paralytic	8	1				10	1			
Puerperal fever§	244	36	16	0		216	29	13	2	2
Scarlet fever	719	32	118	23	35	1,387	89	189	44	37
Tuberculosis:										
Respiratory	937	97	189	37				148	28	
Non-respiratory	149	8	30	4				27	4	
Whooping-cough	2,381	98	356	49	50	3,461	247	384	40	149

DEATHS in Great Towns	1954					1953				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	0	0	0		0
Dysentery	0	0		0		0	0			
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0		0	0	0		
Infective enteritis or diarrhoea under 2 years	9	1	1	2	1	12	2	0	2	2
Influenza	11	1	1	1	1	13	1	4	0	2
Measles			1	0	1		0	0		2
Meningococcal infection		0	0				0	0		
Pneumonia	189	34	20	12	10	164	24	15	11	11
Poliomyelitis, acute	1	0			0	1	0			0
Scarlet fever		0	0	0	0		0	0		0
Tuberculosis:										
Respiratory	87	12	11	1	9	107	14	17	1	8
Non-respiratory			0	1	0		0	3	0	0
Whooping-cough	9	0	0	0	0	0	0	0	0	1
Deaths 0–1 year	226	28	37	9	17	226	31	21	11	40
Deaths (excluding stillbirths)	5,242	750	619	152	191	4,921	653	581	114	187
LIVE BIRTHS	8,009	1227	1008	240	426	8,415	1192	917	261	440
STILLBIRTHS	213	26	32			210	29	27		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Royal College of Surgeons.—At a meeting of the council on May 20, with Sir Cecil Wakeley, P.R.C.S., in the chair, Professor Arthur Steindler (Iowa City, U.S.A.) and Dr. G. Gavin Miller (Montreal) were admitted honorary Fellows, and Mr. J. W. H. Grice, Professor G. Hadfield, Professor J. Trueta, and Mr. W. A. Jackman were elected Fellows. The following prizes and awards were given: *Jacksonian Prize:* Mr. J. H. Peacock (Bristol). *John Tomes Prize:* Professor M. A. Rushton (Guy's). *Moynihan Lectureship:* Professor L. Deloyers (Brussels) and Professor Neils Dungal (Iceland). *Joseph Henry Lectureship:* Dr. R. A. M. Case (London). *Imperial Cancer Research Fund Lectureships:* Dr. J. Bamforth and Dr. E. F. Scowen (St. Bartholomew's). *Begley Prize:* Maurice A. Cowan (Sheffield). Mr. R. S. Handley (Middlesex) was elected and Mr. G. Qvist (Royal Free) re-elected members of the Court of Examiners for a period of three years.

The monthly dinner of the Royal College of Surgeons on May 19 was the first to be held in the new Great Hall, a graceful room in the building risen from the debris of war ruins. Many of the College's Fellows have given the chairs that furnish the hall. Their names appear on the backs of them, and as the President, Sir Cecil Wakeley, said, all the great names in British surgery are inscribed there. Sir Cecil welcomed the guests, and in particular Sir Bernard and Lady Dawson from New Zealand. In reply Sir Bernard said he had often wondered what were the components of the force that pulled them back to London from overseas, and he found part of the answer in this kind of occasion, in the opportunity it gave of meeting their colleagues again. Mr. Geoffrey Keynes, recently appointed the first honorary curator of the College's pictures, then gave a short discourse on them illustrated by lantern slides. Chiefly portraits, they were intimately bound up with the history of the College. The most famous of them, ascribed to Holbein, showed Henry VIII giving the Act of Union to the barbers and surgeons. The College had paid 50 guineas for it in 1786. The portrait of John Hunter in old age, by Reynolds, was now said to be a sombre ghost of what it had been, owing to Reynolds's practice of mixing bitumen with his paint. It had yet been declared by Sir Gerald Kelly, P.R.A., to be the best portrait in England. Mr. Keynes ended by showing some slides of paintings from the Hunter collection depicting abnormal human beings and exotic animals.

Mosquito Control.—A full account is given of the habits and distribution of British species of mosquitoes and of the best measures of controlling them in the revised *Memorandum on Measures for the Control of Mosquito Nuisances in Great Britain* (H.M.S.O., 1s. 3d.). The revision is by Sir Gordon Covell and Mr. P. G. Shute. *Anopheles atroparvus* is believed to be the only species responsible in Britain for indigenous malaria. It is largely confined to the coastal areas in east and south-east England, whence nearly all indigenous cases have been reported.

Parke, Davis & Co.'s new research and administration building at Hounslow was opened on May 20 by the Mayor of Heston and Isleworth in the presence of many distinguished guests representing the medical profession, the pharmaceutical industry, and the Ministry of Health.

"Family Doctor."—The June issue of *Family Doctor* presents its readers with a separate "Summer Beauty Book" as well as articles on such diverse topics as the psychology of war (by Dr. J. R. Rees), diabetes (by Dr. R. D. Lawrence), and travel sickness (by Dr. Alan Porter). Some of the many problems that mothers experience in rearing their children are also discussed and neatly solved.

Changing Trends in the Chest Service.—In a lecture recently given at the Royal Institute of Public Health and Hygiene Dr. Philip Ellman gave some interesting figures showing how the work of tuberculosis dispensaries had changed over the course of the past 20 years or so. As long ago as 1929 he had succeeded in changing the title of the East Ham Tuberculosis Dispensary to "Chest Clinic" because of the opprobrium connected with the former term in the mind of the public. The total attendances had risen from 2,398 in 1928 to 27,521 in 1953, while the proportion of those found tuberculous had fallen from 28.5% in the former year to 5.8% in the latter. The majority of the other 94.2% of the patients were found to be free from disease, and among the remainder were cases of almost every other disease in general medicine, including every type of acute or chronic inflammatory lung disorder, new growths, especially carcinoma of the lung in males, and heart disease. Dr. Ellman's figures underlined his warning against any tendency to develop the tuberculosis service on narrow lines of specialization: prevention, diagnosis, treatment, and after-care must be considered as a continuous process. The chest clinic, situated within the parent hospital, should be itself one department of a whole chest service.

Oxford Graduates' Medical Club.—Founded in 1884 with the object of maintaining associations with the University and promoting good fellowship among members, the club has now extended membership to lady graduates. The life subscription is one guinea. The club dines twice a year, and the summer dinner will be held on July 2 at 7 p.m. in Oriel College, Oxford, with Mr. Ogier Ward in the chair. Guests may be invited. Tickets at 32s. 6d. may be obtained before June 26 from Mr. Selwyn Taylor, 3, Roedean Crescent, Roehampton, London, S.W.15.

B.M.A. Scholarships.—The following research scholarships have been awarded by the B.M.A. for 1954–5: Ernest Hart Memorial Scholarship (£250) to Dr. R. M. Acheson for research into radiological methods in tuberculous meningitis, to be carried out at the Radcliffe Infirmary, Oxford. Walter Dixon Memorial Scholarship (£250) to Mr. G. W. Taylor for research into lymphoedema, at St. Bartholomew's Hospital. Ordinary Research Scholarship (£200) to Dr. I. J. MacQueen, of Sheffield University, for research into radiological methods in tuberculous progressive resistance exercise.

Leverhulme Award.—A Leverhulme research grant has been made to Mr. S. G. Browne, a medical missionary in the Belgian Congo, for the training of medical auxiliaries there.

R.A.M.C. Dinner.—The medical officers of the 56 (London) Armoured Division (T.A.) held their first annual dinner at the Naval and Military Club on May 18. The A.D.M.S., Colonel J. A. Dudgeon, was in the chair, and Brigadier A. L. Crockford, honorary colonel, was also present. Among the principal guests who attended were Major-General D. Dawnay, Major-General B. C. H. Kimmins, Major-General A. Sachs, Colonel Walter Moursand, Jr. (American Medical Services), Dr. S. Morley, Master of the Apothecaries, and Mr. Ronald Champness, of the Worshipful Company of Spectacle Makers.

Sheffield University.—Mr. R. P. Jepson has been appointed to the chair of surgery in succession to Professor R. St. Leger Brockman. Dr. J. M. Thoday is appointed from October 1 head of a new department of genetics.

Royal College of Obstetricians and Gynaecologists.—At a meeting of the council on May 22, with Mr. A. A. Gemmell, P.R.C.O.G., in the chair, the following were elected to the council:—*Representatives of Fellows:* Professor H. H. Evers, Newcastle-upon-Tyne; Professor C. H. G. Macafee, Belfast; Mr. T. N. MacGregor, Edinburgh; Professor W. C. W. Nixon, London. *Representatives of Members:* Mr. I. McG. Jackson, London; Mr. R. Murdoch, Glasgow; Dr. J. Walker, Aberdeen.

Welsh Anaesthetists.—The Society of Anaesthetists of South Wales on April 9 elected the following officers for the year:—*President*: Dr. D. S. Jones. *Vice-president*: Mr. F. Y. Pearson. *Treasurer*: Dr. D. K. W. Picken. *Secretary*: Dr. H. G. Middleton.

Royal Sanitary Institute.—At the annual general meeting on May 18 Dr. A. Scott, M.O.H. of London County Council, and Dr. J. W. Starkey, M.O.H. of Kingston-on-Thames, were re-elected to the council of the Institute.

COMING EVENTS

Contraceptive Technique.—A lecture and demonstration will be given by Dr. Marie Stopes at the Mothers' Clinic, 108, Whitfield Street, London, W.1, on June 3, at 2.30 p.m. Tickets must be obtained in advance.

Leprosy.—An exhibition on leprosy by Dr. R. G. Cochrane will be shown at the Institute of Dermatology on June 7–26.

Brussels Meeting.—A medical conference will be held in Brussels on June 11–15 under the presidency of Professor Pol Gérard. Themes to be discussed include the treatment of pulmonary tuberculosis, liver diseases, and virus diseases. Excursions and other entertainments are offered. Full details from Secrétariat Général, Rue Belliard, 141, Brussels.

Industrial Health.—Dr. M. W. Goldblatt will give the Mackenzie Industrial Health Lecture, entitled "Research in Industrial Health in the Chemical Industry," on July 19 at 2.30 p.m. in the library theatre, Manchester, with Dr. J. A. L. Vaughan Jones in the chair. This is a biennial lecture, organized by the B.M.A. in memory of Mr. James Mackenzie, the founder of the Industrial Health Education Society.

NEW ISSUES

Journal of Neurology, Neurosurgery, and Psychiatry.—The new issue (Vol. 17, No. 2) will be available in a week's time. The contents include:

MENINGIOMAS WITHIN THE LATERAL VENTRICLE. A. E. Wall.
ISCHAEMIC SENSORY LOSS IN PATIENTS WITH PERIPHERAL NERVE LESIONS. R. W. Gilliatt and T. Grahame Wilson.
MEMORY DISTURBANCES IN THIRD VENTRICLE TUMOURS. Moyra Williams and Joe Pennybacker.
VARIATIONS IN THE NUMBER OF ACTIVE PALMAR DIGITAL SWEAT GLANDS WITH AGE. Pamela C. B. MacKinnon.
PHOSPHATE ESTERS IN MYOTONIC HUMAN MUSCLE. P. C. Caldwell and T. A. J. Prankerd.
A RARE PRE-SENILE DEMENTIA ASSOCIATED WITH CORTICAL BLINDNESS (HEIDENHAIN'S SYNDROME). A. Meyer, Denis Leigh, and C. E. Bagg.
TWO CASES OF CONGENITAL ATRESIA OF THE FORAMINA OF MAGENDIE AND LUSCHKA. A. F. J. Maloney.
AUTONOMIC CHANGES FOLLOWING UNILATERAL LEUCOTOMY. Alick Elithorn, Malcolm F. Piercy, and Margaret A. Crosskey.
A COMPARISON OF ISONIAZID WITH MODIFIED INSULIN THERAPY IN NEUROTIC STATES. Maurice Silverman.
RAPIDLY PROGRESSIVE CEREBRAL DEGENERATION WITH MENTAL DISORDER, FOCAL DISTURBANCES, AND MYOCLONIC EPILEPSY. D. P. Jones and S. Nevin.
BOOK REVIEWS.

Issued quarterly; annual subscription £2 2s.; single copy 12s. 6d.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

Journal of Clinical Pathology.—The new issue (Vol. 7, No. 2) is now available. The contents include:

THE USE AND LIMITATIONS OF FILTER-PAPER ELECTROPHORESIS. N. H. Martin and G. T. Franglen.
THE ESTIMATION OF γ-GLOBULIN. George Discombe, Raymond F. Jones, and D. P. Winstanley.
SIMPLIFIED ESTIMATION OF CALCIUM IN BIOLOGICAL MATERIALS BY FLAME PHOTOMETRY. J. G. Llaurado.
A STUDY OF THE BLOOD PYRUVIC ACID LEVEL IN PATIENTS WITH CONGESTIVE HEART FAILURE. J. Kleeberg and S. Gitelson.
MALIGNANT CELLS IN CEREBROSPINAL FLUID. Arthur I. Spriggs.
A CASE OF ANOREXIA NERVOSA WITH NECROPSY FINDINGS AND A DISCUSSION OF SECONDARY HYPOPITUITARISM. R. R. Wilson.
THE STRUCTURAL FEATURES OF EPILOIA WITH SPECIAL REFERENCE TO ENDOCARDIAL FIBROELASTOSIS. L. Crome.
CEREBRAL MUCORMYCOSIS. F. Kurrein.
FURTHER EXPERIENCE WITH THE MALE-TOAD PREGNANCY TEST USING EUROPEAN SPECIES. Magnus Haines, H. P. Ferreira, J. W. Law, and Audrey May.
A STRAIN OF STAPHYLOCOCCUS RESISTANT TO FIVE ANTIBIOTICS. Kevin Anderson.
A NOTE ON THE SEROLOGY OF SARCOSPORIDIOSIS AND TOXOPLASMOSIS. F. I. Awad and R. Lainson.
STREPTOMYCIN-DEPENDENT VARIANTS OF BACT. COLI ISOLATED FROM PATIENTS DURING TREATMENT WITH STREPTOMYCIN. Aksel Stenderup.
THE USE OF A BILE-AESCULIN MEDIUM AND OF MAXTED'S TECHNIQUE OF LANCEFIELD GROUPING IN THE IDENTIFICATION OF ENTEROCOCCI (GROUP D STREPTOCOCCI). Alexander Swan.
THE ERYTHROCYTE SEDIMENTATION RATE AND THE PLASMA VISCOSITY. Robert D. Eastham.
ASSOCIATION OF CLINICAL PATHOLOGISTS: 52nd GENERAL MEETING.

Issued quarterly; annual subscription £2 2s.; single copy 12s. 6d.; obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Applications should be made first to the institution concerned.

Monday, May 31

EDINBURGH UNIVERSITY.—At Physiology Class Room, University New Buildings, 5 p.m., Dr. D. J. Guthrie: Primitive Medicine and its Influence.
EDINBURGH UNIVERSITY: FACULTY OF MEDICINE.—At Obstetrics Lecture Theatre, 60, George Square, 5 p.m., Macarthur Postgraduate Lecture by Professor Bruce Mayes (Sydney): Experiences in the Management of Pregnancy Toxaemia in Sydney.
INSTITUTE OF CARDIOLOGY.—9.30 a.m., Sir John Parkinson: Palpitation.
●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Hammersmith Hospital, 3 p.m., Professor J. Louw (Capetown): Eclampsia.
INSTITUTE OF PSYCHIATRY.—5.30 p.m., lecture-demonstration by Dr. E. Stengel.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., Dr. O. G. Edholm: Effects of Environment in Man.
ROYAL EYE HOSPITAL.—5.45 p.m., Miss J. M. Dollar: Films on Operative Surgery (2).

Tuesday, June 1

EDINBURGH UNIVERSITY: FACULTY OF MEDICINE.—At Anatomy Lecture Theatre, University New Buildings, 5 p.m., Macarthur Postgraduate Lecture by Dr. J. W. Clegg: Surgical Pathology of Pulmonary Tuberculosis.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. P. D. Samman: Reticuloses.
●INSTITUTE OF NEUROLOGY.—5.30 p.m., Dr. R. N. Ironside: Arteritis.
ORPINGTON HOSPITAL.—4 p.m., Dr. P. L. Mollison: Blood Transfusion—Indications and Contraindications.
WRIGHT-FLEMING INSTITUTE OF MICROBIOLOGY.—5 p.m., Almroth Wright Lecture by Professor H. B. Maitland: Histamine-sensitizing Property of *H. pertussis*.

Wednesday, June 2

INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. H. Haber: Necrobioses and Erythema Elevatum Diutinum.
●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Queen Charlotte's Hospital, 12 noon, Professor J. Louw (Capetown): Rupture of the Uterus.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Arris and Gale Lecture by Professor David Slome: Physiological Studies on the Nasal Circulation.

Thursday, June 3

EDINBURGH UNIVERSITY.—At Physiology Class Room, University New Buildings, 5 p.m., Dr. D. J. Guthrie: The Hippocratic School: The Apprenticeship Idea.
●FOOD EDUCATION SOCIETY.—At 16, Berkeley Street, W., 3 p.m., meeting on Milk and Health. Speakers, Professor H. D. Kay, D.Sc., F.R.S., Dr. J. G. Davis, D.Sc., and Mr. W. R. Trehane, M.Sc.
HONYMAN GILLESPIE LECTURE.—At University New Buildings, Edinburgh, 5 p.m., Dr. F. S. Fiddes: Alcohol and Road Safety: The Role of the Doctor in Examining Suspected Car Drivers.
●INSTITUTE OF NEUROLOGY.—5.30 p.m., Mr. Valentine Logue: Injuries to Cranial Nerves.
●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Chelsea Hospital for Women, 3 p.m., Professor J. Louw (Capetown): Urethral Pathology as it Affects the Gynaecologist.
ST. ANDREWS UNIVERSITY.—At Physiology Department, Dundee, 5 p.m., Professor U. S. von Euler (Stockholm): Functional Relationship Between the Suprarenal Medulla and the Adrenergic System.
ST. GEORGE'S HOSPITAL MEDICAL SCHOOL.—5 p.m., neurology demonstration by Dr. J. H. Paterson.
ST. JOHN'S HOSPITAL DERMATOLOGICAL SOCIETY.—4.30 p.m., (1) Demonstration and discussion of clinical cases. (2) Annual general meeting.

Friday, June 4

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., clinical demonstration by Dr. G. B. Dowling: Scleroderma.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Mr. E. F. Chin: Surgery of Acquired and Congenital Defects of the Diaphragm.
UNIVERSITY COLLEGE HOSPITAL MEDICAL SCHOOL.—4 p.m., Holme Lecture by Professor H. K. Beecher (Harvard, Mass.): Drug Induced Changes in Sensation.
WHIPPS CROSS HOSPITAL MEDICAL SOCIETY.—8.30 p.m., Dr. W. Burridge: Excitation and Inhibition.

APPOINTMENTS

EAST ANGLIAN REGIONAL HOSPITAL BOARD.—J. M. Salmon, M.B., B.Ch., Assistant Chest Physician, Great Yarmouth and Lowestoft Chest Clinic Area; Mrs. Heather J. Lopert, L.R.C.P.&S.Ed., Anaesthetic Registrar, Peterborough Memorial Hospital; R. I. H. Welsh, M.B., B.Ch., Surgical Registrar, Peterborough Memorial Hospital; R. C. MacGillivray, M.B., Ch.B., F.R.F.P.S., D.P.M., Consultant Psychiatrist, Little Plumstead Hospital; J. B. Hickey, M.B., B.Ch., Registrar in Ophthalmology, Norfolk and Norwich Hospital; J. H. Jennings, M.B., Ch.B., Surgical Registrar, Stamford and Rutland Hospital; T. J. K. Merritt, M.B., B.S., Registrar in Psychiatry, St. Andrew's Mental Hospital; M. E. York-Moore, M.B., B.S., D.Obst.R.C.O.G., Registrar in Psychiatry, Hellesdon Mental Hospital

HAGAN, J. G., M.B., B.Ch., D.P.H., Deputy Medical Officer of Health and Deputy Principal School Medical Officer, Northampton County Borough.

LAURIE, ALEXANDER, M.B., Ch.B., D.P.H., Assistant County Medical Officer of Health for the Derbyshire County Council and Medical Officer of Health for the Borough of Ilkeston and the Urban Districts of Alfreton and Ripley.

LIVERPOOL REGIONAL HOSPITAL BOARD.—A. R. Carrado, M.D., T.D.D., Whole-time Medical Director of No. 2 Mass Mobile Radiography Unit; E. H. Strach, M.D., M.Ch.Orth., F.R.C.S., Whole-time Assistant Orthopaedic Surgeon to Clatterbridge General Hospital; J. R. Bryson, M.B., Ch.B., F.F.A. R.C.S., Consultant Anaesthetist to Clatterbridge General Hospital; Edith M. Thorp, M.B., Ch.B., D.P.M., Whole-time Assistant

Psychiatrist to Winwick Hospital; D. M. Prinsley, M.D., Senior Resident Medical Officer to Barrowmore Hospital.

MURRAY, FRANCIS J. A., L.R.C.P.&S.I., D.P.H., Medical Officer of Health, Stone Rural District Council, Staffordshire; became medical officer of health for Stone Urban District Council in February, 1953.

NORTH-WEST METROPOLITAN REGIONAL HOSPITAL BOARD.—R. E. Kelly, M.D., M.R.C.P., Consultant Neurologist, Mount Vernon Hospital, Northwood, Middlesex. G. Osborne, M.D., M.R.C.P., D.M.R.D., Consultant Diagnostic Radiologist, Whittington and New End Hospitals. S. H. Harrison, F.R.C.S.Ed., L.D.S. R.C.S.Ed., Consultant Assistant Plastic Surgeon, Mount Vernon Centre for Plastic Surgery and Jaw Injuries. H. W. A. Baron, M.Chir., F.R.C.S., Consultant Surgeon, Hornsey Central Hospital. J. Rubie, M.D., M.R.C.P., D.C.H., Consultant Paediatrician at Hospitals in Windsor Group and at King Edward Memorial Hospital, Ealing. Doreen Nightingale, M.S., F.R.C.S., Consultant Surgeon, National Temperance Hospital. T. M. Moylett, M.B., B.Ch., D.P.M., Assistant Psychiatrist (S.H.M.O.), Three Counties Hospital.

SOUTH-WESTERN REGIONAL HOSPITAL BOARD.—D. I. Rees, B.M., B.Ch., D.L.O., D.A., General-practitioner Anaesthetist (two sessions) at Stroud General Hospital, Gloucester; Joan R. Collins, M.B., Ch.B., General-practitioner Anaesthetist (two sessions) at Newquay and District Hospital; H. J. Doran, M.B., B.Ch., D.L.O., Clinical Assistant in Ear, Nose, and Throat Surgery (two sessions) in the Exeter Clinical Area; W. L. Burrowes, M.D., M.R.C.P.I., Clinical Assistant in General Medicine (one session) at Royal United Hospital, Bath; Irene P. Rowlands, F.R.F.P.S., M.R.C.P., M.R.C.P.Ed., Geriatrician (S.H.M.O.) to North Gloucestershire Clinical Area; B. R. Little, M.R.C.S., L.R.C.P., F.F.A. R.C.S., D.A., Consultant Anaesthetist in Bristol Clinical Area (Weston-super-Mare); G. F. Trobridge, M.B., Ch.B., Registrar in Diseases of the Chest at Hawkmoor Chest Hospital, Bovey Tracey, S. Devon; L. G. Tulloch, M.D., Senior Registrar in Dermatology in Bristol Clinical Area; D. E. Truscott, M.B., B.S., D.M.R.D., Consultant Radiologist to West Cornwall Clinical Area based at West Cornwall Hospital, Penzance; C. D'Arcy Laidlaw, F.R.C.S. Surgical Registrar, Southmead Hospital, Bristol; Rhona E. Morgan, M.B., B.Ch., D.Obst.R.C.O.G., D.C.H., Medical Registrar at Cheltenham General Hospital; J. H. Fox, M.B., Ch.B., D.P.H., Registrar in Diseases of the Chest, Bristol Clinical Area; M. J. Catton, M.B., B.S., Registrar in Pathology at Southmead Hospital, Bristol.

WESTON, JOSEPH W., M.R.C.S., L.R.C.P., D.T.M.&H., Whole-time Assistant Pathologist (S.H.M.O.), Halifax Group, Leeds Regional Hospital Board. (*Corrected announcement.*)

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Ansell.—On May 19, 1954, at the Liverpool Maternity Hospital, to Beatrice (formerly Dubow), B.Sc., wife of Abraham Ansell, M.D., D.M.R.D., a daughter.

Baker.—On May 13, 1954, to Dr. Hazel Baker (formerly Hill), wife of Mr. J. A. C. Baker, M.A., of Wednesbury, Staffs, a third son—Francis William.

Eastcott.—On May 16, 1954, at Iver, Bucks, to Bobby, wife of Mr. H. H. G. Eastcott, M.S., F.R.C.S., a daughter.

Garretts.—On May 10, 1954, at the British Military Hospital, Iserlohn, B.A.O.R., 24, to Sheila Ruth (formerly Hirschfield), wife of Captain Maurice Garretts, M.B., M.R.C.P., R.A.M.C., a daughter—Angela Edelle.

Hewitt.—On May 18, 1954, at Bristol Maternity Hospital, to Yvonne, wife of Dr. Keith M. Hewitt, a son.

O'Sullivan.—On May 13, 1954, at Doriscourt Nursing Home, Manchester, to Una, wife of Dr. J. G. O'Sullivan, a son—Timothy Francis.

MARRIAGES

King—Watts.—On April 10, 1954, at the Cathedral of the Highlands, Nairobi, Kenya, Anthony John King, B.Sc., F.G.S., of Wallasey, Cheshire, to Anne Wendy Watts, M.B., B.S., of Newcastle-upon-Tyne.

DEATHS

Bradlaw.—On April 19, 1954, at 8, Hatherley Court, Bayswater, London, W., David Barnett Bradlaw, L.R.C.P.&S.I.&L.M., aged 79.

Collins.—On April 14, 1954, at Virginia Water, Surrey, Michael Abdy Collins, O.B.E., M.D., of Saxmundham, Suffolk, aged 75.

Elliott.—On April 20, 1954, at 82, Stepney Road, Scarborough, John Lewis Elliott, L.M.S.S.A., late of Cudworth, Yorks, aged 81.

Fardon.—On April 19, 1954, at 23, Rose Hill, Dorking, Surrey, Albert Henry Fardon, M.D., D.P.H., aged 76.

Gilchrist.—On April 9, 1954, at the North Staffordshire Royal Infirmary, Stoke-on-Trent, Adam Gilchrist, M.B., Ch.B., of Bleak Hill House, Burslem, Stoke-on-Trent, aged 68.

Glynn.—On March 28, 1954, at his daughter's home, 76, Hawthorne Crescent, Stoke Poges Lane, Slough, Bucks, John Joseph Glynn, L.R.C.P.&S.I. & L.M., late of 159, Old Street, London, E.C.

Hammond.—On April 20, 1954, at the Royal Hospital, Wolverhampton, John Hammond, M.B., Ch.B., of Fantaisie, Albert Road, Wolverhampton.

Heath.—On April 6, 1954, Thomas Lowthian Heath, M.R.C.S., L.R.C.P., of Thornton Heath, Surrey, aged 62.

Henderson.—On April 8, 1954, in hospital, David Henderson, M.D., late of Cheddleton, near Leek, Staffs.

Hoyten.—On April 4, 1954, William James Hoyten, M.D., D.P.H., aged 86.

Jones.—On April 7, 1954, at Camberley, Surrey, David Elgan Eiddig Jones, M.B., F.R.C.S.

Lowson.—On April 6, 1954, at Wendover, Bucks, James Prain Lowson, M.D.

Marcus.—On November 28, 1953, in Trinidad, British West Indies, Emil W. Marcus, M.D.

Mayberry.—On April 2, 1954, at 92, Holden Road, Finchley, London, N., Robert John Mayberry, M.B., Ch.B.

Mills.—On April 10, 1954, at Orpington Hospital, Frederick André Mills, M.B., B.Ch., late of 20, The Drive, Sevenoaks, Kent, aged 84.

Nickerson.—On April 10, 1954, at Cour Kintyre, Argyll, William Henry Snyder Nickerson, V.C., C.B., C.M.G., M.B., Ch.B., D.P.H., Major-General, late R.A.M.C., retired, aged 79.

Peel.—On April 12, 1954, at Glenthorne, Staircase Lane, Bramhope, Yorks, John Percival Peel, M.B., B.S., aged 53.

Stanley.—On April 8, 1954, at St. Leonards-on-Sea, Sussex, Hubert Stanley, M.B., B.Ch., aged 90.

Sturrock.—On April 4, 1954, Herbert Moncrieff Sturrock, L.R.C.P.&S.Ed., L.R.F.P.S., F.D.S. R.C.S.Ed., of 28, Melville Street, Edinburgh.

Vivian.—On April 4, 1954, at Westaway Drive, Bexhill-on-Sea, Sussex, Harold Sugden Vivian, M.B., B.S., D.O.M.S.

Any Questions?

What is Fibrositis?

Q.—*(1) What is fibrositis? What are the nodules which clinicians feel, or profess to feel, in the affected tissues? What are the so-called trigger zones? (2) What is the relationship between fibrositis and emotional stress and osteoarthritis of the spine?*

A.—(1) Fibrositis is in large measure a medical myth. It is loosely applied to pain felt in the musculo-skeletal system for which a more exact nomenclature cannot be found. One of the most common types is pain associated with an anxiety neurosis (the so-called "psychogenic rheumatism" of the Americans). As commonly used, the term includes also pain due to subacromial bursitis, pain arising in tendons and ligaments as the result of chronic or acute trauma, postural pain, pain arising from disk lesions, and pain arising through pressure on sensitive structures such as nerves in the thoracic inlet. The nodules which are to be felt in this condition are usually normal fatty lobules; like any other structure, they may be the site of referred pain and tenderness. They are palpable in certain areas of the back in many people without fibrositis. There is no histological proof of any specific lesion in the muscles or connective tissue that justifies the name of "fibrositis." Trigger areas are those areas in which pressure produces radiating or referred pain.

(2) The relationship between fibrositis and emotional stress or strain is often a direct one. People in a disordered psychological state are often more aware of the ordinary aches and pains of everyday life and particularly more aware of any pain due, for instance, to postural disorders. Osteoarthritis of the spine is something that occurs in everyone with increasing age. However, when this is discovered radiologically it is frequently blamed for pain in the back. It may sometimes be the cause of it if the abnormal bony proliferation interferes with movement and the function of the spinous ligaments.

Storage of Oxygen Cylinders

Q.—*In this district we propose to have oxygen for emergency cases kept by the local pharmacist. Can you kindly tell me what are the dangers of explosion? Can an oxygen cylinder be left stored in a room with a gas or open fire? We propose to use a B.L.B. mask. Can this be used in a room with a gas, electric, or coal fire?*

A.—The risk of stored oxygen cylinders exploding is practically negligible. Where there is no alternative, an oxygen cylinder may be left in a room with an open fire, so long as the cylinder is placed as far from the fire as possible and shielded so that it does not become unduly hot. It is better, however, that cylinders should be stored under proper conditions, as outlined in British Standard 1319, 1946. It is dangerous to use oxygen therapy near an open fire because in the presence of oxygen inflammable objects catch fire more easily and burn more vigorously. If the use of oxygen with a B.L.B. mask is imperative in these circumstances, the patient and cylinder should be placed as far from the fire as possible and good ventilation of the room ensured. An oxygen tent is never permissible in the vicinity of an open fire.

Rosehip Syrup

Q.—*Can you provide a recipe for making rosehip syrup so that it retains a high content of vitamin C?*

A.—A good recipe may be found in the leaflet "Hedgerow Harvest," which was issued by the Ministry of Food. Two pounds (0.9 kg.) of hips are put through a coarse mincer, and at once placed in three pints (1.7 litres) of water which has been kept briskly boiling in readiness. The water is again brought to the boil, and the saucepan is then

put aside to cool for 15 minutes. The water and hips are next poured into a jelly-bag made of flannel or linen, crushed, and allowed to drip until most of the fluid has come through. If the first drippings from the jelly-bag contain hairs from the insides of the hips they are put back into the bag. When the flow of fluid has ceased the hips are returned to the saucepan and are stirred up with another 1½ pints of boiling water. After standing for 10 minutes they are put back into the jelly-bag and more fluid is collected. The combined extracts are boiled down to a volume of 1½ pints, and a final boiling of five minutes is given after the addition of 1½ lb. of sugar. While still hot the syrup is poured into small bottles, which must be hot and sterile. If they are sealed with corks these should be boiled for a quarter of an hour just before use, and should be covered with melted paraffin wax.

About two teaspoonfuls of the extract should supply a daily dose of vitamin C. The syrup should be stable if kept in full bottles in a cool darkened cupboard, but the vitamin deteriorates in a few weeks after the bottles have been opened and air admitted. Cooking utensils made of copper or uncovered iron should not be used for making the syrup, since these metals accelerate the destruction of vitamin C.

Intraperitoneal Transfusion of Infants

Q.—*When anaemic infants who are in no immediate danger from anoxia need blood transfusions, I have found the following technique useful in tropical practice. The freshly collected blood is injected into the peritoneum. If no sodium citrate or heparin should be available, fresh blood may be used, clotting being prevented by contact with the peritoneum. A 50- or 20-ml. syringe is satisfactory, provided one works quickly and leaves the needles in situ during the proceedings. The blood haemoglobin rises within a few days, and the procedure may be repeated at short intervals. Do you commend this technique? During the first few minutes of life, is it safe to use the mother's blood for this purpose without grouping?*

A.—There is plenty of evidence that when red cells are injected intraperitoneally the majority eventually find their way into the blood stream. However, the process is relatively slow, and may not be complete one week after the injection. In practice the procedure appears to be fairly safe, since some authors have given quite large numbers of intraperitoneal blood injections to children without observing any ill-effects. Nevertheless, it cannot be considered as safe as an ordinary transfusion nor can it be considered so efficient.

During the first two or three months of life the only antibodies present in the infant's serum are those derived from the mother by placental transfer. Thus, at this time, the mother's red cells can be injected into the infant without any risk of a haemolytic reaction. However, it has to be remembered that the mother may be Rh-positive and the infant Rh-negative, so that there is a possibility of sensitizing the infant to the Rh antigen. In the case of female infants this is a serious matter, since sensitization to the Rh antigen, once established, persists indefinitely; therefore tests must always be made to ensure that Rh-positive blood is not given to an Rh-negative recipient.

Carbon Dioxide Bubbles on Acidifying Urine

Q.—*When clearing phosphatic urine with acid is there a production of visible bubbly carbon dioxide?*

A.—When a urine is very alkaline, as in alkalosis produced by taking excess of alkali-forming salts, there will be sufficient carbonate present to give rise to visible carbon dioxide formation on the addition of acid. The usual cause of evolution of carbon dioxide on acidifying is that the urine is stale and bacterial decomposition of the urea has formed a considerable amount of ammonium carbonate which gives a marked evolution of gas on acidifying.

Can a Doctor Practise as a Vet?

Q.—*Can a doctor legally practise veterinary surgery for payment without a veterinary qualification?*

A.—No person may practise veterinary surgery, whether for payment or otherwise, unless his name is entered in the *Register of Veterinary Surgeons* or the *Supplementary Veterinary Register*. The only exceptions to this rule are: (1) Treatment given to an animal by its owner or a member of his household or his employee; (2) anything done otherwise than for reward by a person engaged in agriculture to an animal owned for the purpose of agriculture; (3) the rendering in emergency of first aid for the purpose of saving life or relieving pain; (4) the destruction of any animal by painless methods; and (5) the castration of certain young animals, the tailing of a lamb, the docking of a dog's tail, or the amputation of its dew claws before its eyes are open.

Bleary Eyes

Q.—*A young man of 26 in otherwise excellent health and with perfect eyesight complains that his eyes are persistently rather bleary and bloodshot, especially in the morning, at which time he finds it difficult to face bright light without his eyes watering. On examination, his eyes are slightly bloodshot (although not nearly so markedly, he states, as in the morning). What is the likely cause and what treatment is recommended?*

A.—The most likely explanation is that he is suffering from slight conjunctivitis together with a greater than average sensitiveness to bright light. Another possible factor is that his lacrimal glands secrete excessive tears on relatively slight provocation. It should be remembered that the visibility of the superficial vessels of the conjunctiva varies from person to person, even in the absence of inflammatory changes. Exposure to dust and to irritating vapours, including tobacco smoke, is a frequent cause of conjunctival injection. If this young man's eyes are actually inflamed, an attempt should be made to find out whether he is exposed to any avoidable irritant, and then treat the conjunctivitis on general principles if it should persist after elimination of the probable source of irritation.

NOTES AND COMMENTS

Infection from the Chalice.—Dr. LILIAS M. JEFFRIES (Hove) writes: In your issue of May 8 (p. 1107) under "Any Questions?" is a full and useful reply on infection from the chalice, but it states that "in fact no instance of transmission by this means has ever been substantiated." The following incident is within my recollection. It occurred in the Christian village church of Clarkabad in the Punjab, India, about 30 years ago. The English head of the C.M.S. mission, who was on a visit there, was the celebrant. One of the congregation developed hydrophobia shortly after communicating, and died. Later, one or possibly two others were also affected. The celebrant was severely infected and died. No doubt these facts are recorded and could be verified in the Church Missionary Society's records.

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